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Volume 60 Number 709
January 1987

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and its application to risk assessment

THE BRITISH JOURNAL OF RADIOLOGY

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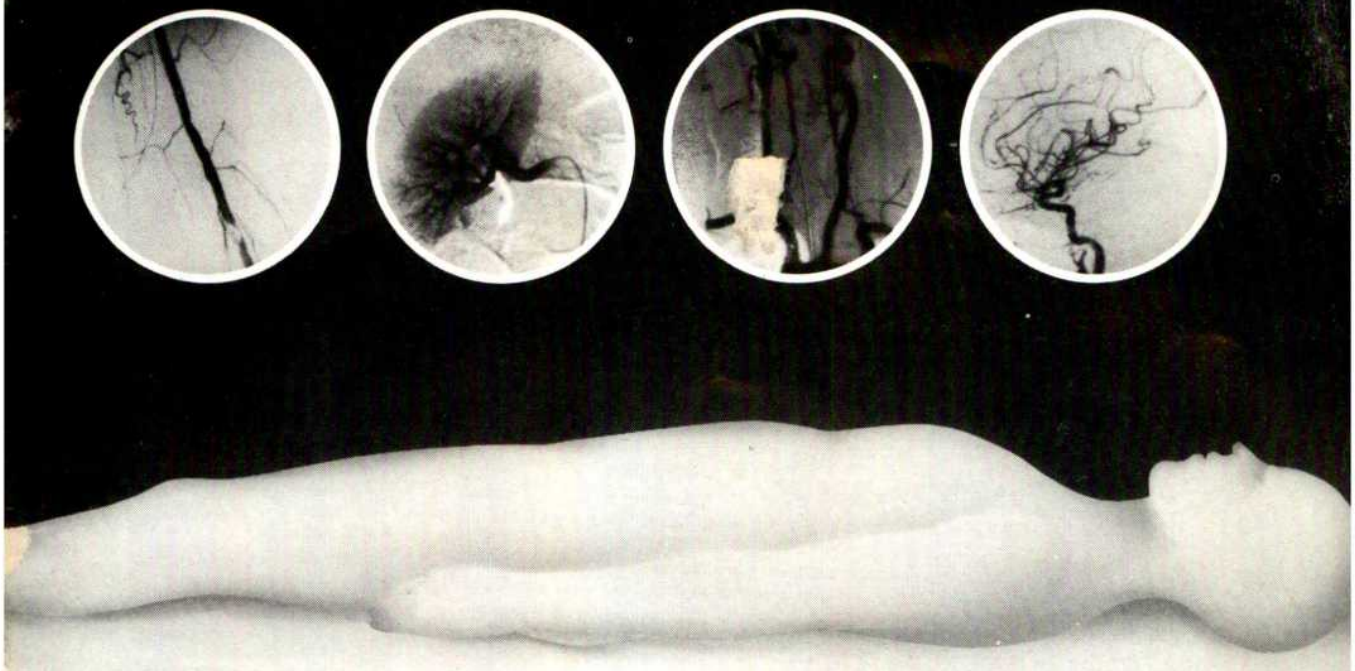

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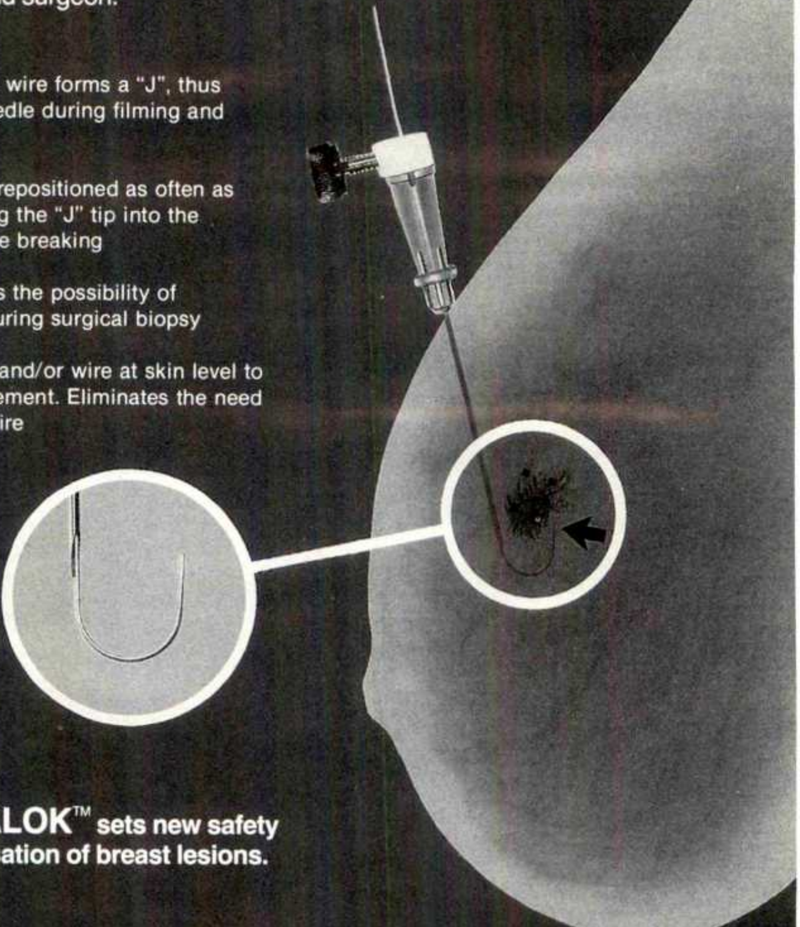

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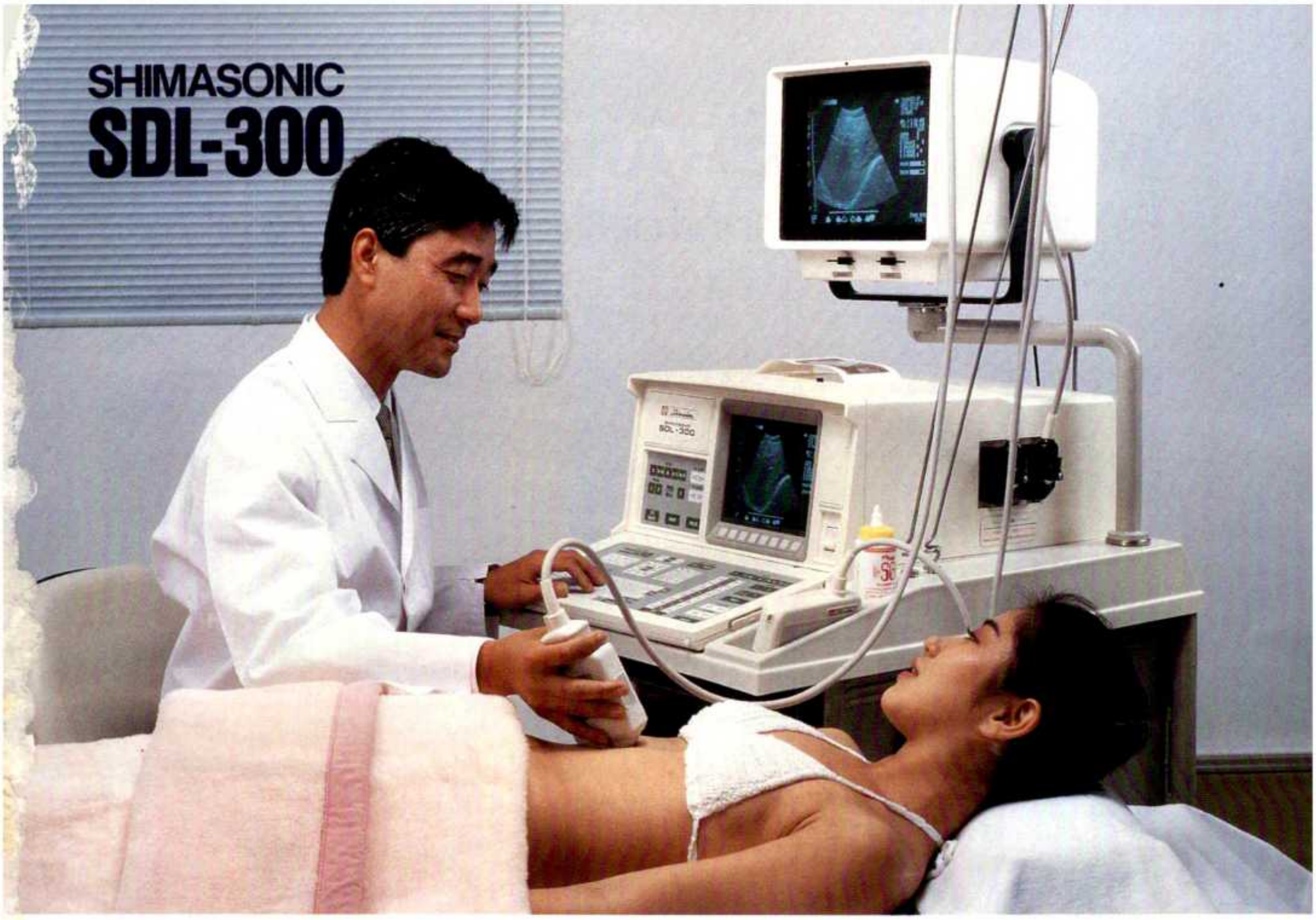

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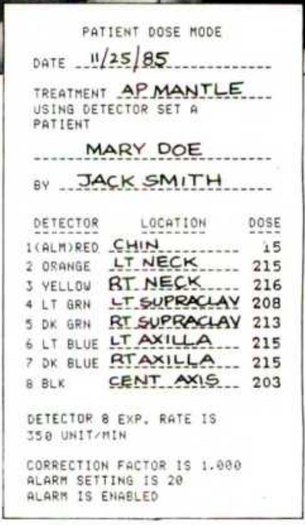

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          PATIENT DOSE MODE

DATE  11/25/85
TREATMENT  AP MANTLE
USING DETECTOR SET A
PATIENT
         MARY DOE
BY  JACK SMITH

DETECTOR     LOCATION        DOSE
--------     --------        ----
1(ALM)RED   CHIN               15
2 ORANGE    LT NECK           215
3 YELLOW    RT NECK           216
4 LT GRN    LT SUPRACLAV      208
5 DK GRN    RT SUPRACLAV      213
6 LT BLUE   LT AXILLA         215
7 DK BLUE   RT AXILLA         215
8 BLK       CENT AXIS         203

DETECTOR 8 EXP. RATE IS
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CORRECTION FACTOR IS 1.000
ALARM SETTING IS 20
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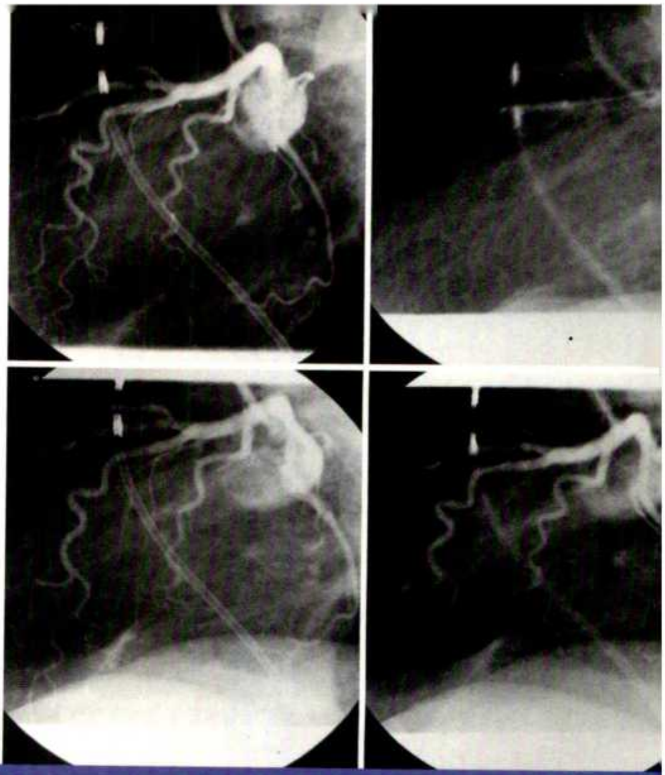

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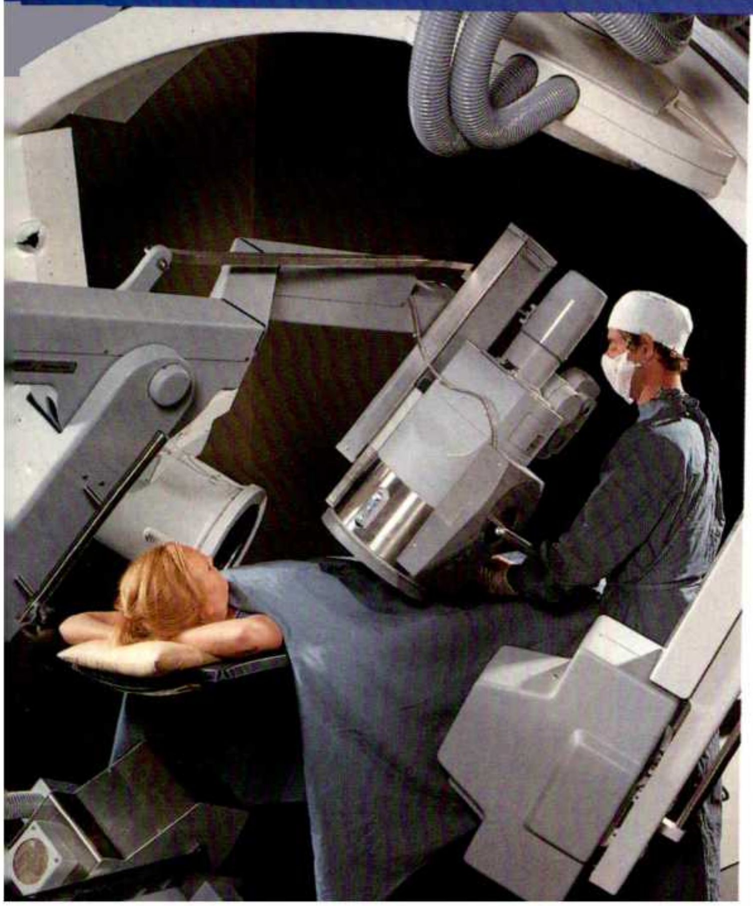

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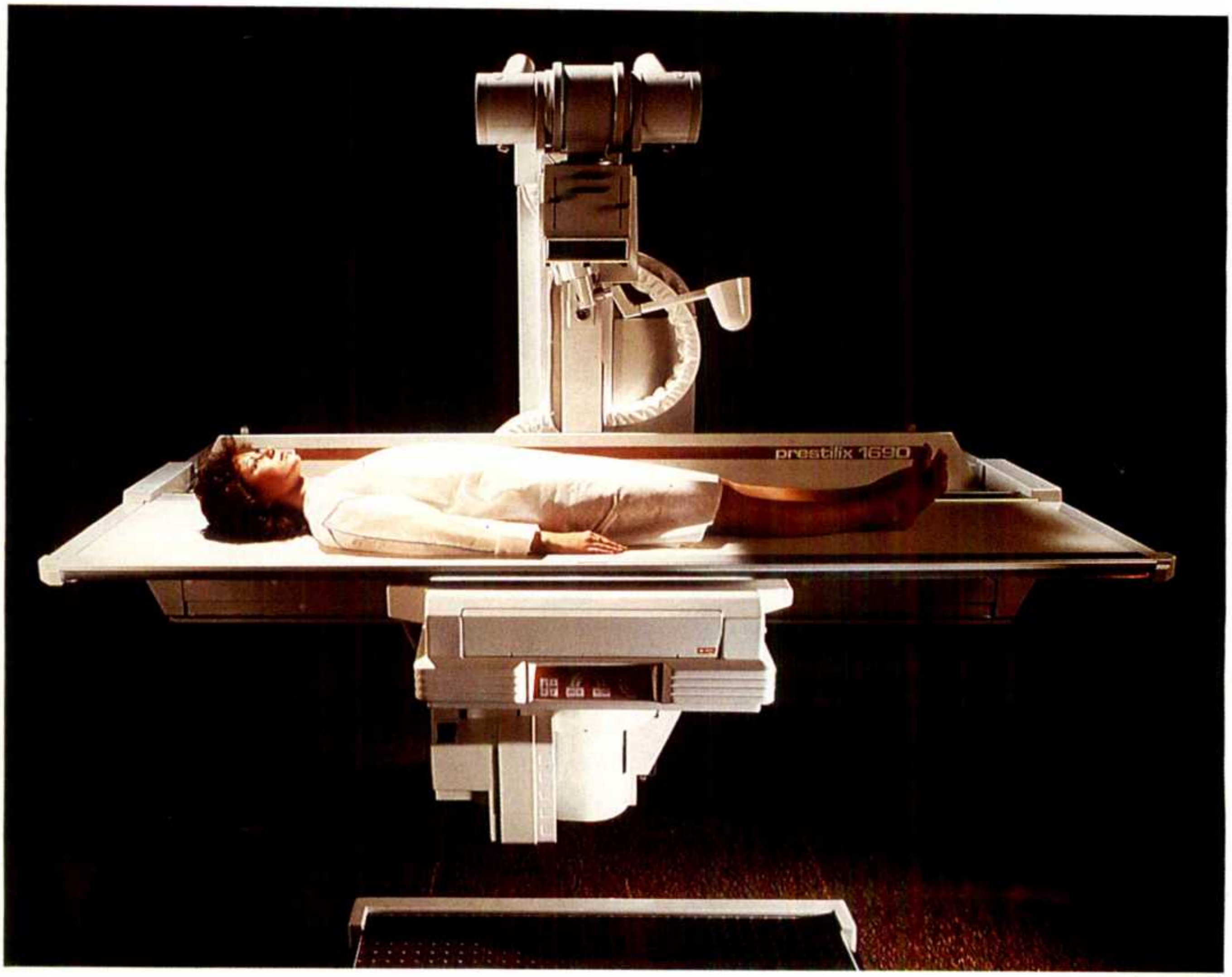

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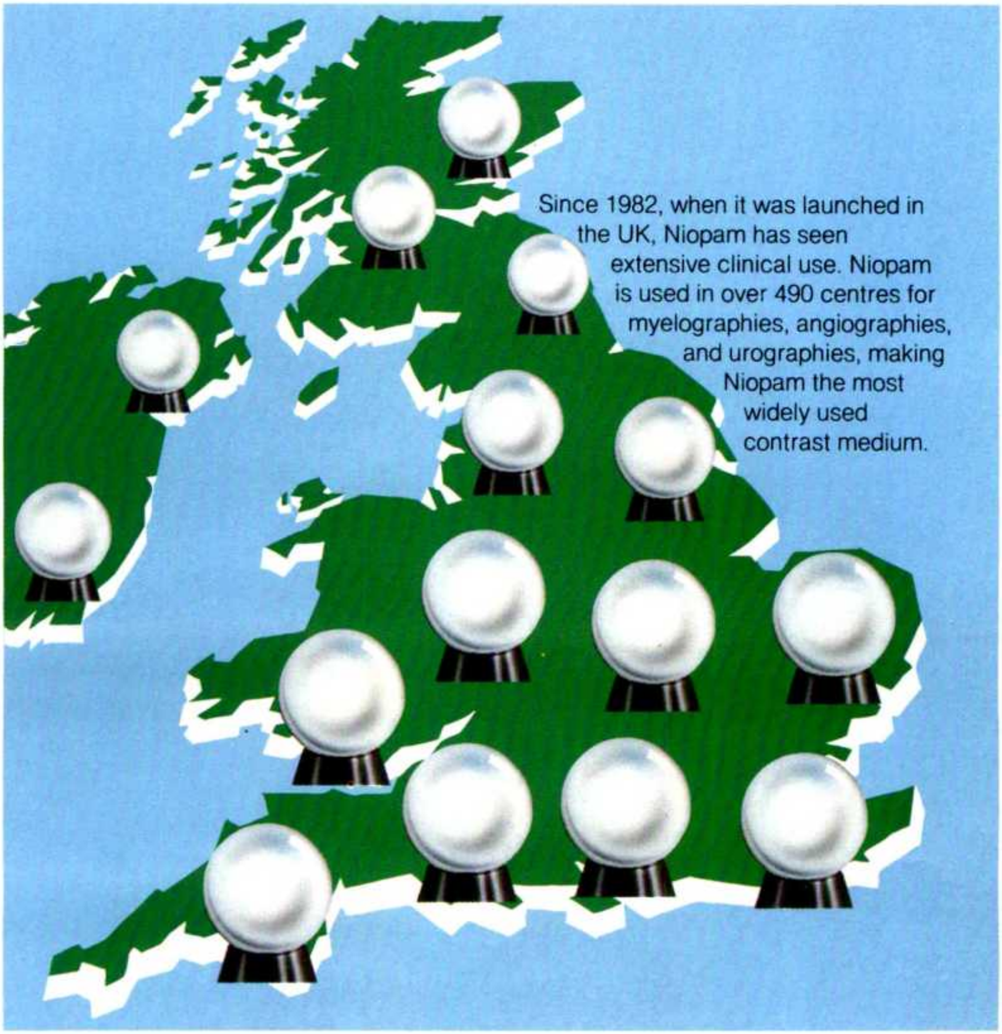

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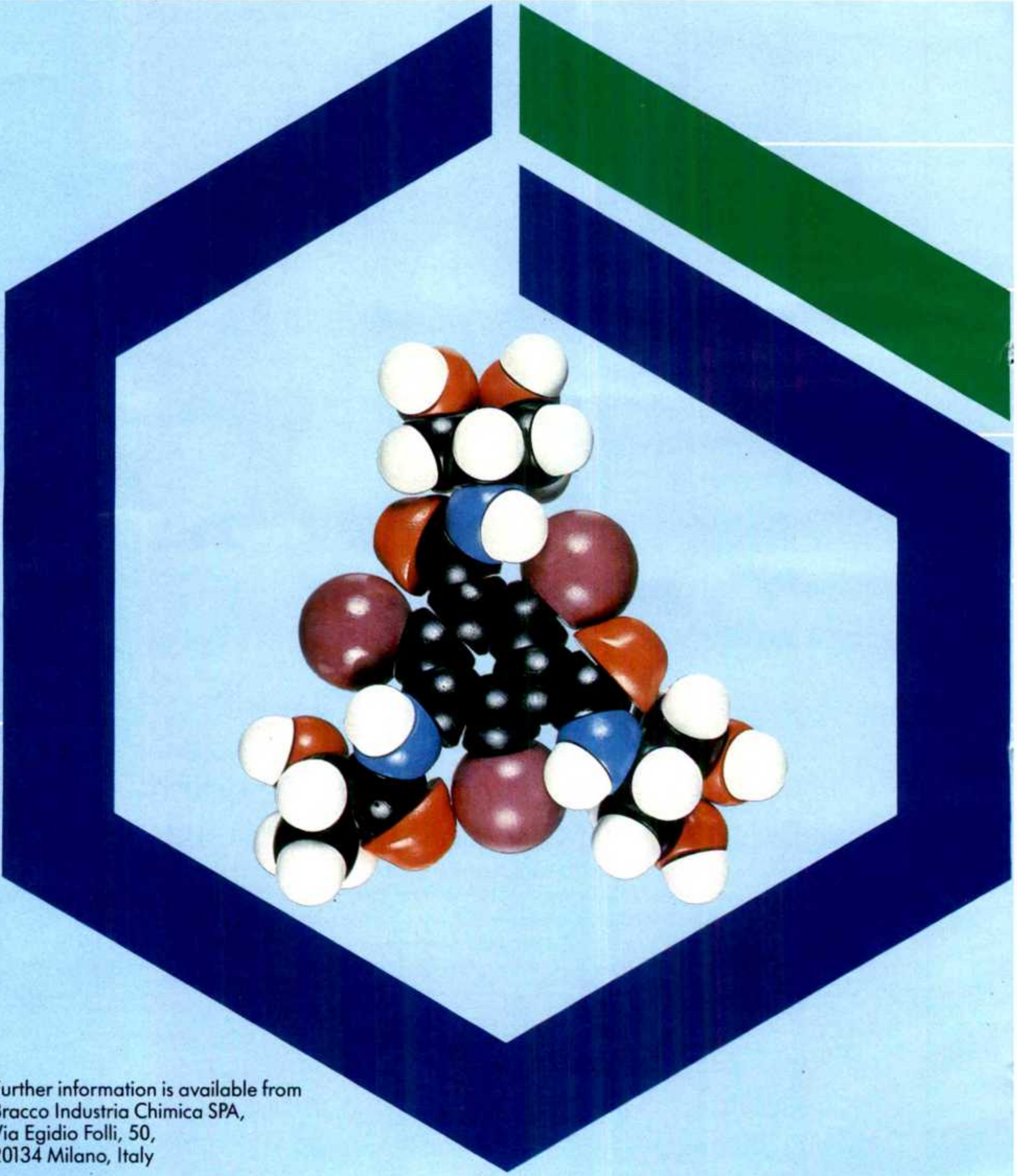

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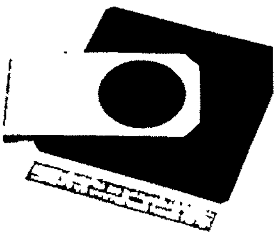

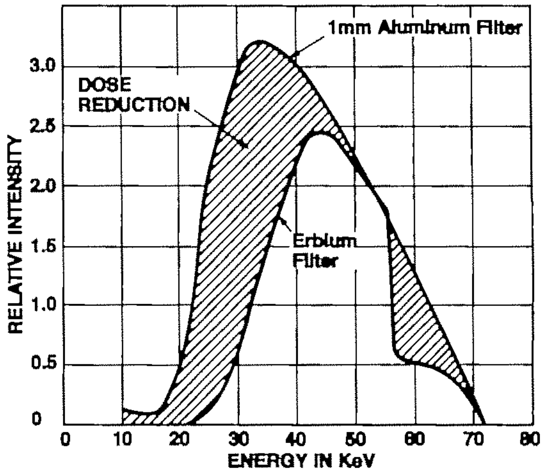

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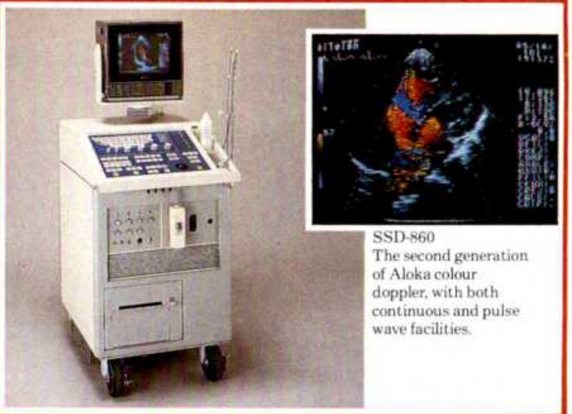

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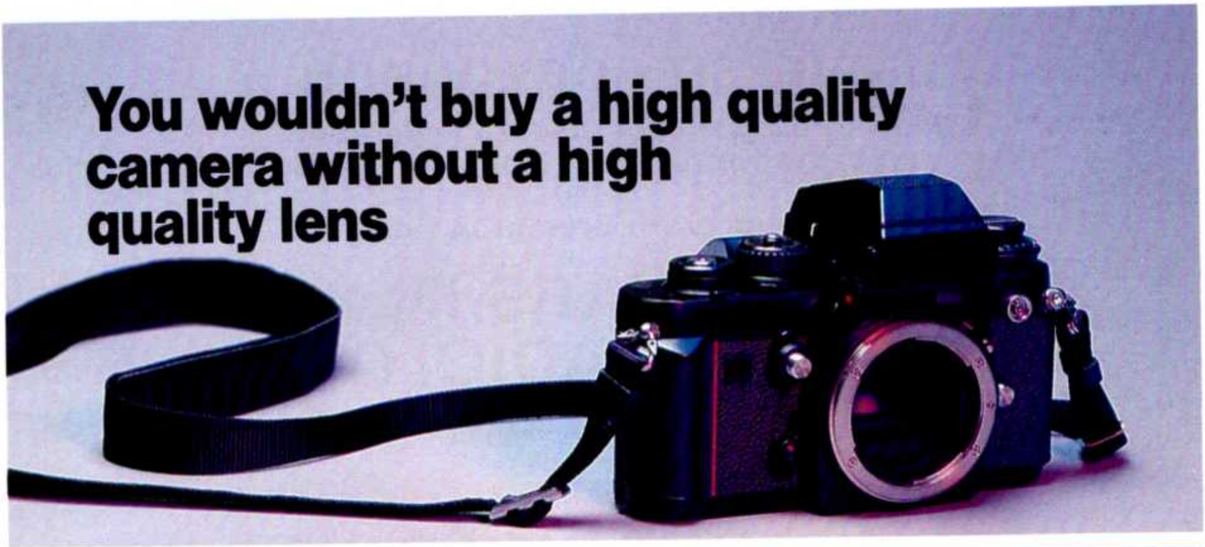

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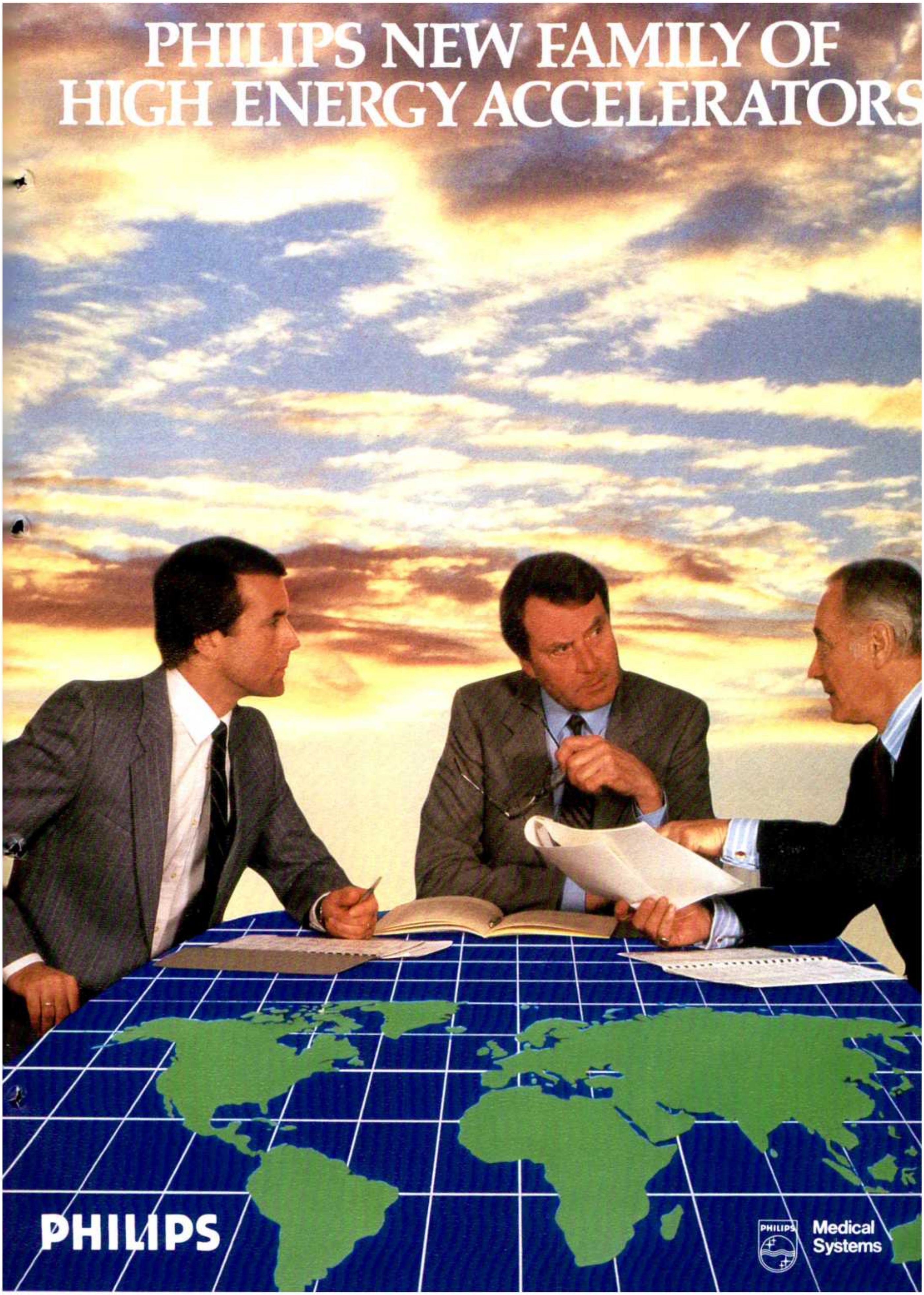

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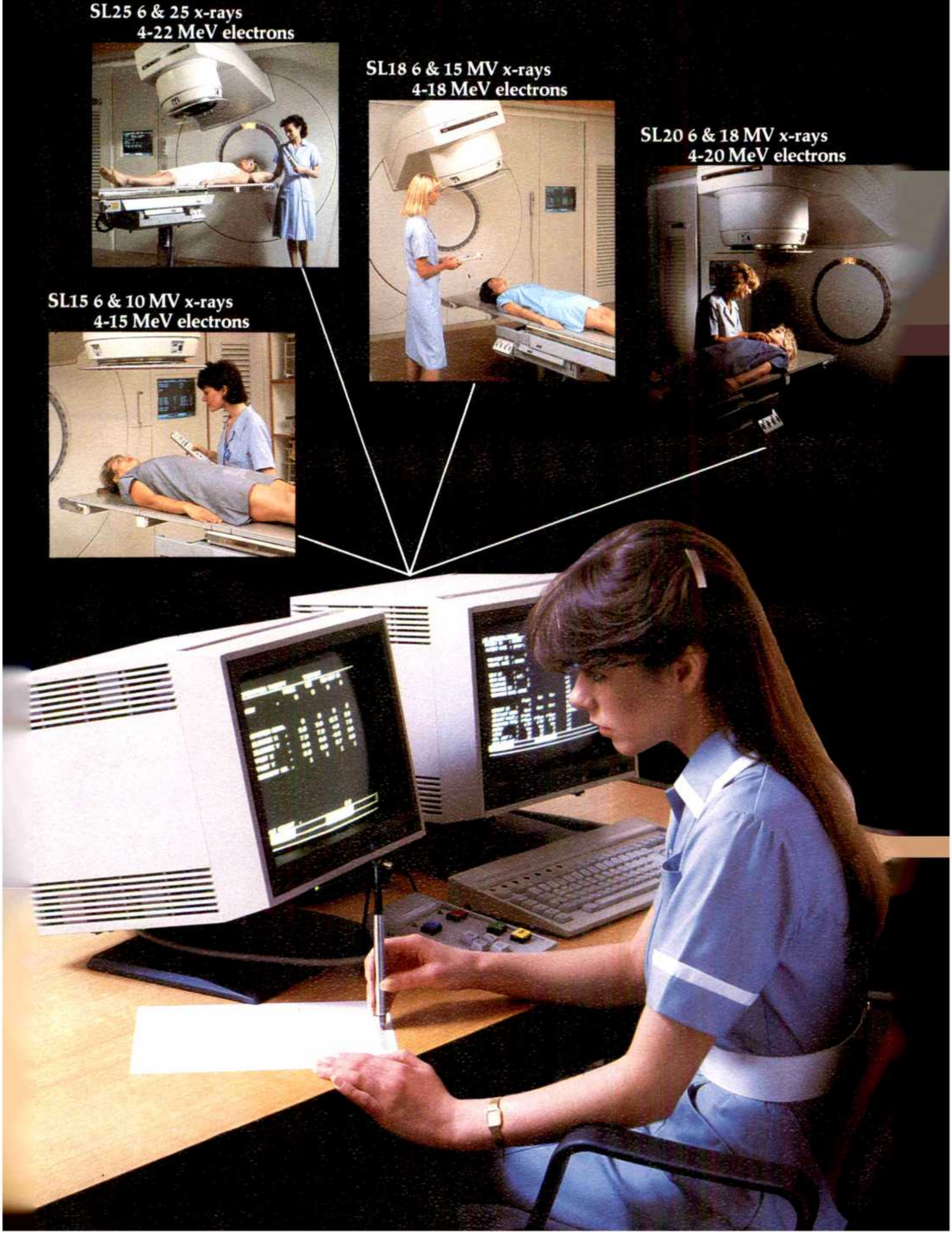

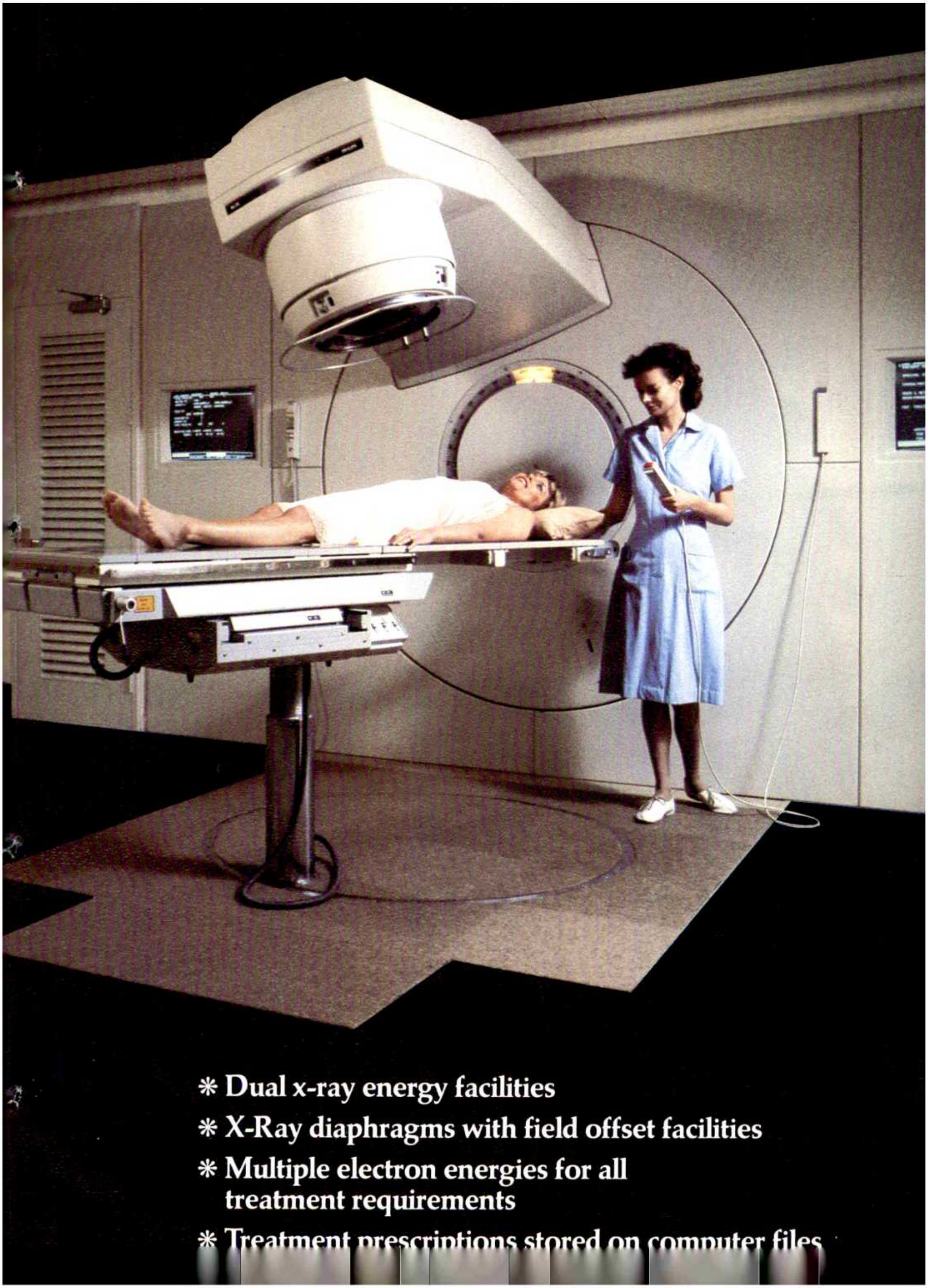

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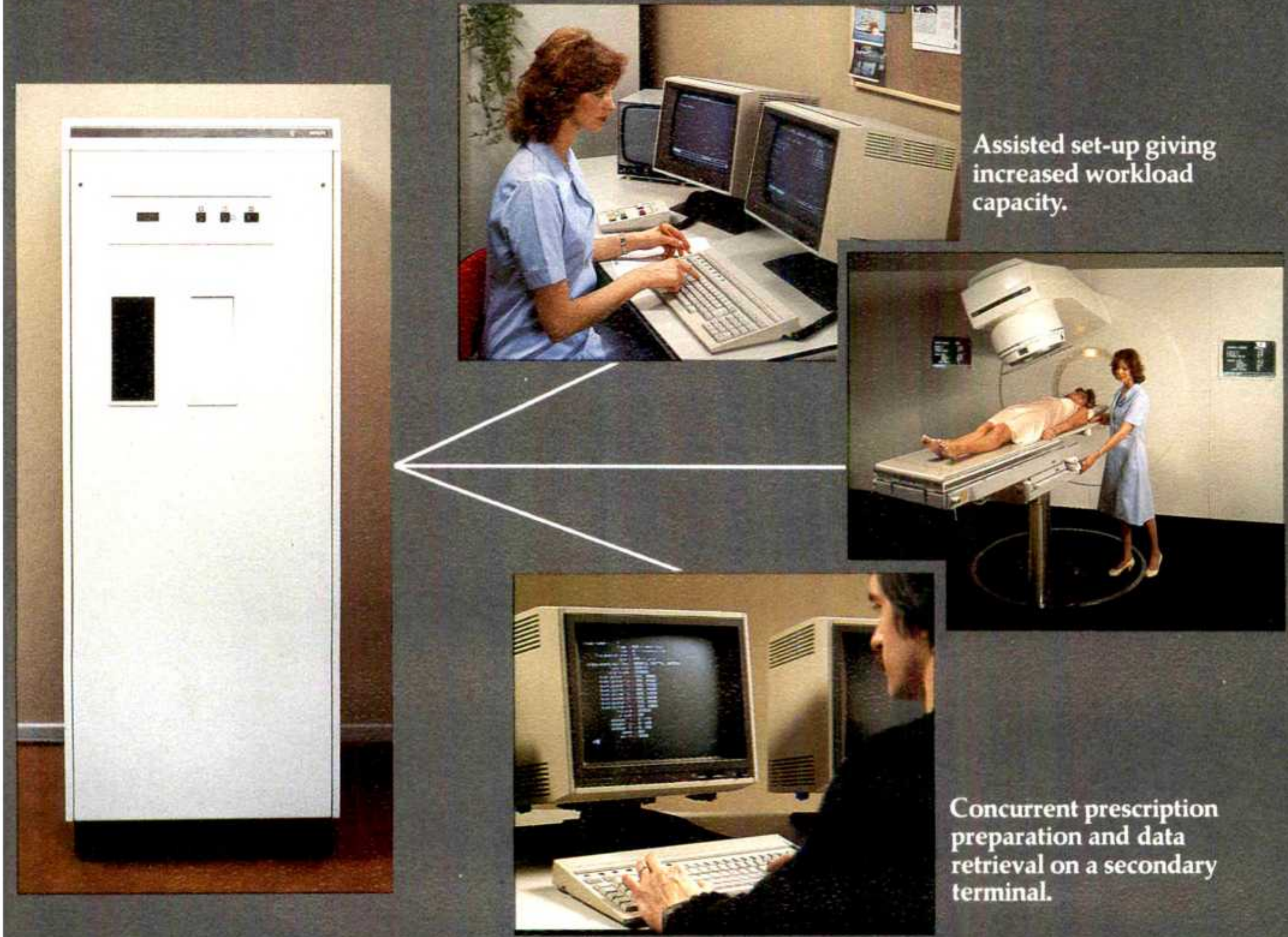

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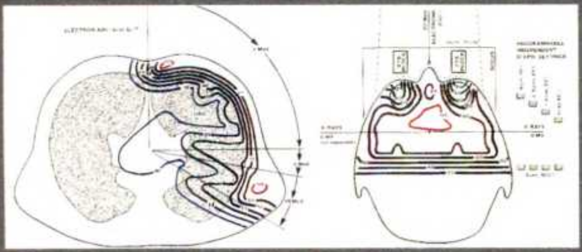

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The British Journal of Radiology

Biological basis of radiological protection and its application to risk assessment

Proceedings of a one-day seminar held at the BIR 44th Annual Congress, Bristol, April 11, 1986

Chairmen: R. J. Berry and F. D. Sowby

Cancer induction and non-stochastic effects

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ABSTRACT

The mechanisms of carcinogenesis are not known in detail, but there is strong evidence that cancer usually arises from a single transformed cell. Hence, although the process of carcinogenesis appears to require a multiplicity of changes in the affected cancer-forming cell, such as may be associated with successive stages of tumour initiation, tumour promotion, and tumour progression, only one such change induced by radiation in an appropriate cell may be conceived to increase the probability of neoplasia in a suitably susceptible individual. For this reason, carcinogenic effects of radiation, like mutagenic effects of radiation, are considered for purposes of radiological protection to have no threshold and to behave as stochastic phenomena. In contrast, certain other effects of radiation, such as cataract of the lens, infertility, and depression of the bone marrow, require the killing of many cells in the affected organs. Thus, they vary in severity with the extent of cell loss and have thresholds of detectability which depend on the sensitivity with which the consequences of cell loss can be measured.

In recommending dose limits for radiological protection, the International Commission on Radiological Protection (ICRP) distinguishes between "stochastic" and "non-stochastic" effects. The former are viewed as probabilistic phenomena which have no threshold and which vary in frequency but not severity with the dose, while the latter are viewed as deterministic phenomena which have thresholds and which vary both in frequency and in severity with the dose (ICRP, 1977).

This report reviews briefly the dose–effect relationships for both types of effects, with particular reference to their compatibility with currently recommended dose limits.

CARCINOGENIC EFFECTS OF RADIATION

Carcinogenic effects are classified as stochastic effects for purposes of radiological protection, in addition to mutations, chromosome aberrations, and teratogenic effects (ICRP, 1977). In principle, each of these types of effect is inducible by injury to only one of the many cells in an affected tissue, in contrast to non-stochastic effects, which require damage to large numbers of cells (Hulse & Mole, 1982). This contrast between the two types of effect in the numbers of cells that must be injured suffices to explain the differences in their assumed dose–effect relationships (*e.g.* Fig. 1).

Mechanisms of carcinogenesis

Modern theories of carcinogenesis view cancer as a monoclonal growth which arises through stepwise alterations in a single cell and its progeny. Although the neoplastic alterations are yet to be defined in molecular terms, the process of carcinogenesis is commonly divided operationally into three stages: initiation, promotion, and progression (Farber, 1984).

Initiation is generally thought to involve some type of heritable change which predisposes the affected cell and its progeny to subsequent neoplastic transformation (Farber, 1984). On the basis of the available information, the frequency of initiation can be inferred to increase as a linear non-threshold function of the dose of low-LET radiation and to be far higher per unit dose than the frequency of mutations at any one genetic locus (Kennedy & Little, 1984; Clifton et al, 1985), implicating multiple oncogenic sites, damage of the

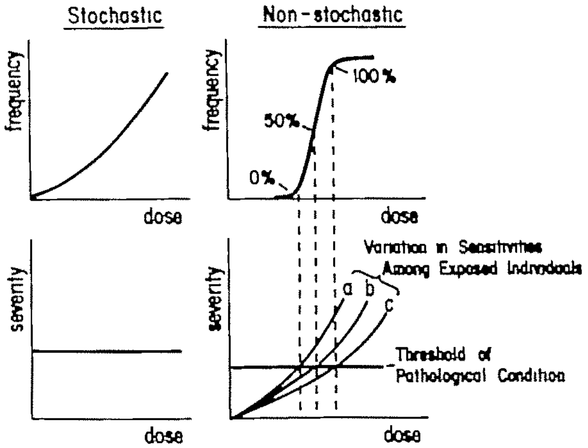


FIG. 1

Differences between characteristic dose–effect curves for stochastic effects and those for non-stochastic effects. The upper and lower figures on the right illustrate how the frequency and severity of a non-stochastic effect increase with dose in a population of individuals who vary in susceptibility; the severity of the effect increases most steeply in those who are of greatest susceptibility (lower figure, curve a), reaching the threshold of clinical detectability at a lower dose in this subgroup than in less susceptible subgroups (curves b and c), the range of dose over which the different subgroups cross the same threshold of severity is reflected in the upper curve, which shows that the frequency of the effect in the entire population reaches 100% only at that dose which exceeds the threshold in all members of the population (from ICRP, 1984).

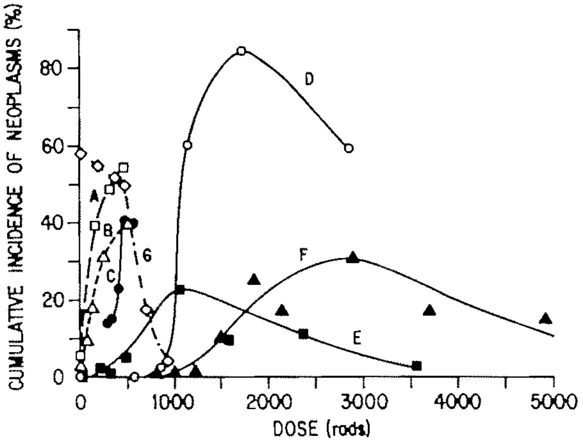


FIG. 2

Dose–incidence curves for different neoplasms in animals exposed to external radiation: (A) myeloid leukaemias in X-irradiated mice (Upton et al, 1958); (B) mammary gland tumours at 12 months in gamma-irradiated female rats (Shellabarger et al, 1969); (C) thymic lymphomas in X-irradiated mice (Kaplan & Brown, 1952); (D) kidney tumours in X-irradiated rats (Maldague, 1969); (E) skin tumours in alpha-irradiated rats (percentage incidence × 10) (Burns et al, 1968), (F) skin tumours in electron-irradiated rats (percentage incidence × 10) (Burns et al, 1968); (G) reticulum cell sarcomas in X-irradiated mice (Metalli et al, 1974). (From Upton, 1984; modified from UNSCEAR, 1972.)

genome at sites unlikely to be repaired, or genetic damage other than point mutations. The specific genes that are involved remain to be identified but may conceivably include anti-oncogenes (Knudson, 1985) as well as oncogenes (Guerrero et al, 1984; Garte et al, 1985). Although the activation of more than one oncogene appears to be necessary for neoplastic transformation (*e.g.* Land et al, 1983), the data imply that initiation may be induced with one-hit kinetics.

Tumour promotion, the process through which the initiated cell and its progeny subsequently undergo the additional change necessary for neoplastic transformation, may involve more than one step and, typically, requires repeated and prolonged exposure to promoting stimuli (Upton, 1982). In contrast to initiation, which is induced at a rate of 0.1-1.0/cell/Gy, the subsequent transforming event that is induced in initiated cells occurs at a rate of only 10^{-6} to 10^{-7} per cell generation (Kennedy & Little, 1984). The molecular mechanism of promotion remains to be determined, but tumour-promoting chemicals have traditionally been thought to act predominantly through epigenetic mechanisms (Weinstein et al, 1984). Recently, however, many such chemicals have been found to be capable of inducing damage to chromosomes and DNA via free radicals or other indirect mechanisms (*e.g.* Cerutti et al, 1983; Upton et al, 1984; Liehr et al, 1985; Troll & Weisner, 1985). Hence, the importance of changes in gene structure, as opposed to changes in gene expression (*e.g.* Rubin, 1980), remains to be defined. Radiation has been postulated to exert promoting effects through the regenerative hyperplasia that it induces by the killing of cells; such a mechanism has been implicated, for example, in the induction of osteosarcomas by bone-seeking alpha-emitters (Marshall & Groer, 1977) and in the induction, through abscopal effects, of thymic lymphomas (Kaplan, 1967), ovarian tumours (Upton, 1967) and thyrotropic pituitary tumours in mice (Furth, 1982).

Tumour progression, which is the process through which successive changes in the cells of a neoplasm give rise to increasingly malignant subpopulations (Foulds, 1969), is yet to be explained in molecular terms; however, mutations and chromosome aberrations have been implicated (Nowell, 1976; Farber, 1984). The process may be accelerated by repeated exposure to radiation or other carcinogenic stimuli, or by selection pressures that favour the outgrowth of increasingly autonomous clonal derivatives.

Dose–incidence relationship

Neoplasms of virtually every anatomical type have been induced in one species or another, but not all types of neoplasms are elicited in any given species or strain.

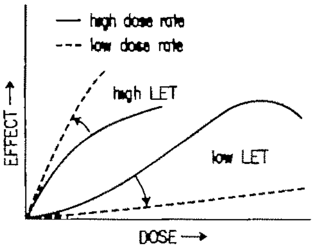


FIG. 3.

Schematic dose–incidence curves for carcinogenesis in relation to dose and dose rate of high-LET and low-LET radiation (from Upton, 1984).

Among the different neoplasms there are wide variations in dose–incidence relationships, and certain types of neoplasms actually decrease in frequency with increasing dose (*e.g.* Fig. 2).

Although some diversity in dose–incidence relationships would be expected in view of the multicausal, multistage nature of carcinogenesis and the fact that the mechanisms of carcinogenic effects are not the same in all instances, the observed variations remain largely unexplained. Clearly, all of the observed dose–incidence curves cannot be represented by the same mathematical function, but the data are consistent with a number of generalisations.

(1) A radiation-induced elevation in the age-specific incidence of a particular neoplasm may or may not result in an increase in the final cumulative incidence of the disease, depending on the survival of the population at risk.

(2) At low doses and low dose rates, the carcinogenic effectiveness of X rays and gamma rays per unit dose is generally reduced, whereas that of high-LET radiation tends to remain constant or may even be increased (Fig. 3) (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1977; Broerse & Gerber, 1982; Upton, 1985).

(3) With many types of neoplasm, the incidence passes through a maximum at an intermediate dose, owing in part to the killing of cells which would otherwise have become malignant (UNSCEAR, 1972), and decreases with further increase in the dose (*e.g.* Fig. 2).

(4) With daily exposures, the median time of tumour appearance (t) tends to vary inversely with the daily dose (d), according to the function:

$$t^n = \frac{C}{d} \qquad (1)$$

where n is greater than 1.0 and C is a constant (Albert & Altshuler, 1973).

(5) Because radiation may influence carcinogenesis through more than one mode of action, at least at high dose levels, the dose–incidence curve may reflect a combination of initiating effects, promoting effects and anticarcinogenic effects, depending on the neoplasm, the dose, and the conditions of exposure.

(6) The interactive effects of radiation in combination with other agents may be additive, synergistic, or antagonistic, depending on the agents, exposure sequence, and dose in question (UNSCEAR, 1982).

(7) At low to moderate dose levels, the effects of radiation generally can be augmented by appropriate tumour-promoting stimuli.

(8) Initiating effects of radiation, when promoted to full expression, generally increase as a linear non-threshold function of the radiation dose (*e.g.* Fig. 4).

(9) Dose–incidence data for cancers in irradiated human populations, although available over a relatively wide range of doses (UNSCEAR, 1977; Committee on the Biological Effects of Ionising Radiation (BEIR), 1980), do not suffice to define the dose–incidence relationship for carcinogenesis in the low dose domain or to exclude the possibility of a threshold.

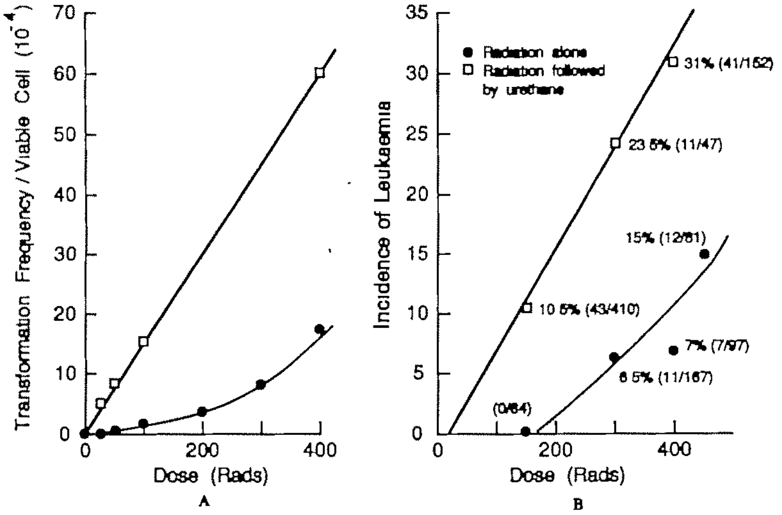


FIG 4.

(A) Dose–response relationship for the induction of neoplastic transformation in mouse 10T1/2 cells by X rays alone (●) or by X rays followed by phorbol ester, starting 48 h after irradiation and continued for the full 6-week expression period (□). Phorbol ester alone caused no increase in transformation frequency (from Little, 1981) (B) Incidence of leukaemia in C57BL mice in relation to the dose of X rays, administered in a single exposure, with and without subsequent injections of urethane Urethane alone produced no leukaemias (reproduced from Berenblum & Trainin, 1963).

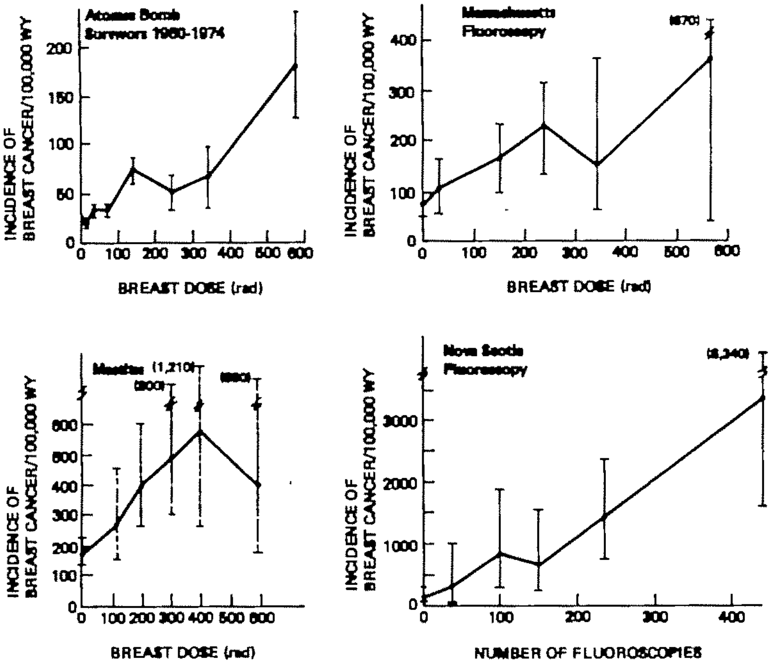


FIG 5.

Incidence of cancer of the female breast as a function of dose in atomic-bomb survivors, women treated with X rays for acute post-partum mastitis, and women subjected to multiple fluoroscopic examinations of the chest during treatment of pulmonary tuberculosis with artificial pneumothorax (from Boice et al, 1979).

(10) The carcinogenic risks associated with low-level exposure can be estimated only on the basis of assumptions about the relevant dose–incidence relationships and mechanisms of carcinogenesis.

Several lines of epidemiological evidence support the assumption of a non-threshold dose–incidence relationship (BEIR, 1980; Rall et al, 1985). Perhaps the strongest lines of evidence are:

(1) the excess of leukaemia and other juvenile cancers that is associated with prenatal X irradiation in the 10–50 mGy range (Monson & MacMahon, 1984; Harvey et al, 1985);

(2) the excess of thyroid tumours that is associated with an average dose of 60–80 mGy to the thyroid gland from irradiation of the scalp for tinea capitis in childhood (Modan et al, 1977; Shore et al, 1980);

(3) the dose-dependent excess of leukaemia in atomic-bomb survivors, which is evident down to doses in the range below 0.25 Gy (BEIR, 1980; Rall et al, 1985); and

(4) the excess of breast cancer, which is similar in magnitude per unit dose (Fig. 5), irrespective of marked differences in the duration of exposure, in (a) women exposed to atomic-bomb radiation, (b) women given therapeutic irradiation for post-partum mastitis, (c) women subjected to multiple fluoroscopic examinations of the chest during the treatment of pulmonary tuberculosis with artificial pneumothorax, and (d) women exposed occupationally to external gamma radiation in the painting of luminous clock and instrument dials (Boice et al, 1979; BEIR, 1980; Baverstock et al, 1981).

Latency and age distribution of radiation-induced neoplasms

Tumours induced by radiation have relatively long latencies, which vary in different species as a more or less constant function of the natural life span (Brues, 1955). Within a given species, the latency varies also with age at the time of irradiation and with the type of neoplasm induced, tending to be shorter for leukaemia than for solid tumours (Upton et al, 1960). Furthermore, long before certain experimentally induced leukaemias are evident clinically, "pre-neoplastic" cells in the affected animals can be detected with appropriate techniques (Haran-Ghera, 1977; Boniver et al, 1981; Hirashima et al, 1982).

The age differences observed in latencies and types of induced leukaemias (Fig. 6) appear to be related in some way to similar age differences in the rates of corresponding "spontaneous" leukaemias (Upton, 1964). In contrast to the risks of leukaemia and of juvenile forms of cancer, in general, which tend to peak within a decade after irradiation and then decrease (Fig. 6), the risks of adult-type malignancies (osteosarcomas excluded) tend to increase progressively with time after irradiation, in parallel with the age-dependent increase in the underlying baseline incidence (Fig. 7). It is noteworthy, for example, that in women irradiated during childhood, radiation-induced carcinomas of the breast do not become evident until the age of 35–40 years, that is, the age at which breast cancer characteristically begins to appear in the general population (Shore et al, 1984; Tokunaga et al, 1984). This long latency implies that carcinogenesis in the

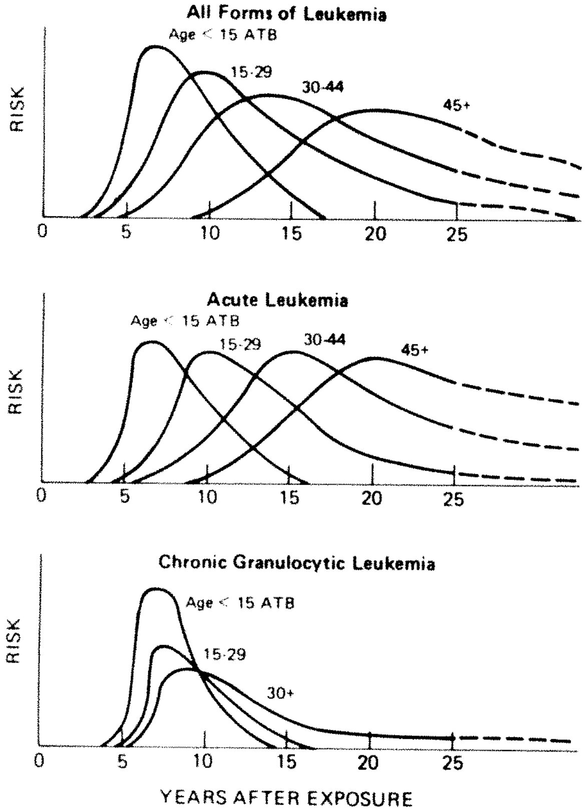


FIG. 6.

Temporal distribution of radiation-induced leukaemias in atomic-bomb survivors, in relation to type of leukaemia and age at the time of irradiation (from Ichimaru & Ishimaru, 1975).

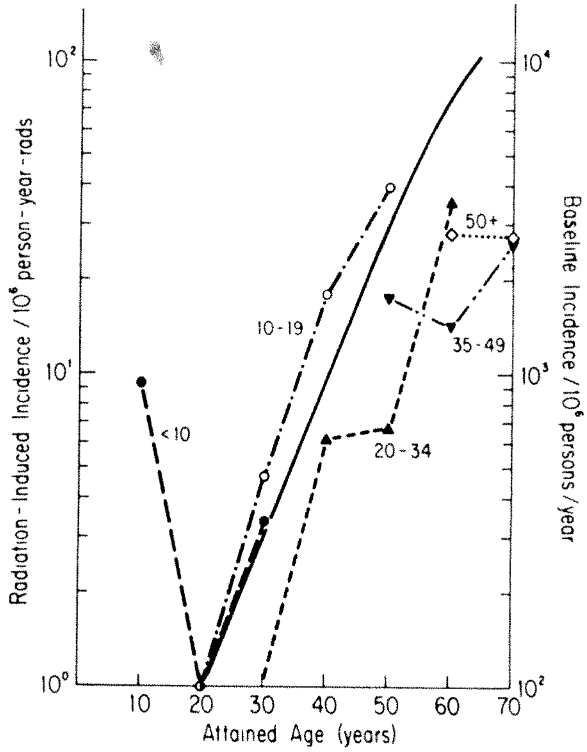


FIG. 7.

Incidence of radiation-induced cancers (excluding leukaemia) in relation to attained age in different birth cohorts of heavily irradiated Nagasaki atomic-bomb survivors, as compared with the baseline incidence in the general population of Japan. Data for atomic-bomb survivors (Wakabayashi et al, 1983) denoted by dashed curves, with age at time of irradiation of each cohort as indicated. Data for the general population (Waterhouse et al, 1976) denoted by the solid curve (from Upton, 1985).

female breast is merely initiated by irradiation and does not develop further without being promoted by age-dependent hormonal stimulation. Since the annual excess of other solid cancers (all types combined) also appears to increase with time as a more or less constant fraction of the underlying baseline incidence (Fig. 7), the data suggest that carcinogenic effects in other organs also are promoted by as yet unidentified age-dependent influences. In this respect, the data largely support the "relative risk" rather than the "absolute risk" projection model (Rall et al, 1985).

Risk estimates for specific organs

From the available epidemiological evidence, the risks of radiation carcinogenesis in various organs have been estimated on the basis of non-threshold interpolation models (Table I). Such estimates imply that the lifetime risks of cancer associated with occupational irradiation at present dose rates are relatively small (*e.g.* Table II).

The extent to which a given cancer arising in an irradiated individual may be attributable to a dose of radiation that he or she received previously cannot be made with confidence, owing not only to unresolved questions about the relevant dose–incidence relationship for carcinogenesis, but also to other sources of uncertainty, such as the potentially confounding effects of inherited differences in susceptibility, exposure to carcinogens other than radiation, and other unknown risk factors, the influence of which cannot be specified. Everything else being equal, however, the probability that a specific cancer resulted from a given dose, *i.e.* the "probability of causation" (PC), can be represented by the expression:

$$PC = R/(1+R) \tag{2}$$

where R denotes the relative excess of cancer in the population referable to the dose in question, calculated on the basis of the appropriate risk model (Bond, 1981; Rall et al, 1985). Although this relationship merely represents the probability of causation for a hypo-

TABLE I

ESTIMATED RISK OF CANCER RESULTING FROM LOW-LEVEL LOW-LET IRRADIATION, IN RELATION TO SITE, SEX, AGE AT EXPOSURE AND TIME AFTER IRRADIATION*

Site	Age at exposure (years)	Years at risk†	Dose–response model	Absolute risk‡	
				Male	Female
Leukaemia (all types except CLL)	0–9	5–26	Linear-quadratic	0.173	0.110
	10–19	5–26		0.0854	0.0543
	20–34	5–26		0.0846	0.0538
	35–49	5–26		0.105	0.0670
	50+	5–26		0.156	0.0990
Salivary gland	0–14	10–30	Linear-quadratic	0.001 04	0.001 04
Oesophagus	20–34	10–30	Linear-quadratic	0.0052	0.0052
	35–39	10–30		0.0084	0.0084
	50+	10–30		0.0224	0.0224
Stomach	10–19	10–30	Linear-quadratic	0.0160	0.0160
	20–34	10–30		0.0308	0.0308
	35–49	10–30		0.0508	0.0508
	50+	10–30		0.134	0.134
Colon	20–34	10–30	Linear-quadratic	0.0208	0.0208
	35–49	10–30		0.0336	0.0336
	50+	10–30		0.0892	0.0892
Liver	20–34	10–30	Linear-quadratic	0.028	0.028
	35–49	10–30		0.028	0.028
	50+	10–30		0.028	0.028
Pancreas	20–34	10–30	Linear-quadratic	0.018	0.018
	35–49	10–30		0.030	0.030
	50+	10–30		0.0788	0.0788
Lung	10–19	10–33	Linear-quadratic	0.030	0.030
	20–34	10–33		0.056	0.056
	35–49	10–33		0.086	0.086
	50+	10–33		0.120	0.120
Breast	0–9	10–35	Linear	—	0.38
	10–19	10–35		—	0.76
	20–29	10–35		—	0.49
	30–39	10–35		—	0.49
	40–49	10–35		—	0.13
	50+	10–35		—	0.08
Kidney and bladder	20–34	10–30	Linear-quadratic	0.0200	0.0200
	35–49	10–30		0.0368	0.0368
	50+	10–30		0.0648	0.0648
Thyroid	0.9	10–34	Linear	0.15	0.50
	10–19	10–34		0.15	0.50
	20–34	10–34		0.05	0.15
	35–49	10–34		0.05	0.15
	50+	10–34		0.05	0.15

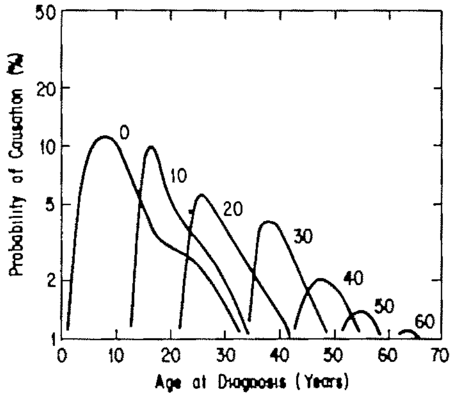
*From Rall et al, 1985.

†Following radiation.

‡Number of cancers per 1000 persons per year per Sv (organ dose) of low-level, low-LET radiation, averaged over the specified period of risk

thetical average member of the population and is of questionable validity for any specific individual, its use has been mandated by the US Congress for assessing compensation claims filed by uranium miners and by US citizens exposed to radioactive fallout from weapons tests in Nevada (Rall et al, 1985). A similar approach also has been proposed for use in assessing the attributable risks of cancers in compensation cases involving occupational exposure to asbestos (*e.g.* Chase et al, 1985). Hence, wider use of this approach may be expected.

From the above formula, used with the risk



(from Rall et al, 1985)

FIG. 8.

Attributable risk ("probability of causation") of leukaemia after exposure to 1 rad, in relation to age at exposure (indicated by number next to curve) and age at diagnosis (data from Rall et al, 1985)

coefficients listed in Table I, it can be calculated that the attributable risk of radiation-induced leukaemia decreases markedly with age at the time of exposure (Fig. 8) and that it would fail to reach 10% at any age in a person exposed annually to 5 mSv per year from age 20 years to age 70 years. From certain rarer cancers, on the other hand, such as those of the liver and thyroid gland, the PC values under the same conditions of irradiation can be calculated to exceed 10% late in life (Rall et al, 1985).

NON-STOCHASTIC EFFECTS

Non-stochastic effects, such as impairment of fertility, cataract of the lens, and depression of haemopoiesis, require doses large enough to damage or deplete many of the cells in affected tissues. If the number or proportion of cells that is damaged remains sufficiently small, no impact on the function of the affected organ is detectable. Conversely, if a large enough number or proportion of cells is damaged, the impact on the function of the organ is severe. Hence, the threshold for the effect may vary, depending on the sensitivity of the method that is used for detecting it. Its threshold also can be expected to vary among individuals who differ in susceptibility (Fig. 1).

Non-stochastic effects include many types of tissue injury, some of which develop more rapidly than others, depending on the conditions of irradiation and the physiology of the tissues in question. In most instances, the effects result predominantly from depopulation and disorganisation of affected organs through interference with the normal renewal of their aging cells. Vascular degeneration, fibrosis, and other mechanisms of injury also may contribute to varying degrees, especially in the pathogenesis of late-occurring effects (Fig. 9).

It is beyond the scope of this report to review the mechanisms of the various non-stochastic effects. These are discussed in depth elsewhere (UNSCEAR, 1982; ICRP, 1984). Nevertheless, radiation-induced changes in cell survival and tissue kinetics are sufficiently important in the pathogenesis of most non-stochastic effects to deserve some comment.

Cell proliferation and tissue kinetics

In general, the rapidity of a tissue's response to irradiation depends on the rate at which its cells are replaced under normal, steady-state conditions, since the killing of dividing cells by irradiation tends to interfere with the timely replacement of the tissue's mature cells as they are lost through senescence or other mechanisms (Fig. 9). Tissues characterised by rapid cell turnover (such as epidermis, bone marrow, intestinal epithelium) typically manifest injury sooner than do tissues characterised by slow cell turnover (*e.g.* liver, kidney, brain) (UNSCEAR, 1982). In the gastrointestinal mucosa it takes only a few days for maximal depletion of epithelial cells after an acute exposure,

TABLE II

ESTIMATES OF LIFETIME CANCER RISKS ATTRIBUTABLE TO OCCUPATIONAL IRRADIATION IN VARIOUS TYPES OF WORK INVOLVING EXPOSURE TO IONISING RADIATION, US, 1975*

Type of work	No. of persons exposed annually	Average annual dose per person (mSv)	Annual collective dose (person-Sv)	Lifetime cancer mortality commitment (fatal cancers)†
Healing arts	500 000	0.80–1.60	400–800	10–20
Manufacturing and industrial	7 000 000	0.07	500	12.5
Nuclear energy	62 000	8.40	520	13
Research	100 000	1.20	120	3
Naval reactors	36 000	2.20	80	2

*From Jablon & Bailar, 1980.

†Estimated numbers of radiation-induced cancers occurring within the lifetimes of the groups shown, based on 1 year's occupational exposure at the dose levels specified.

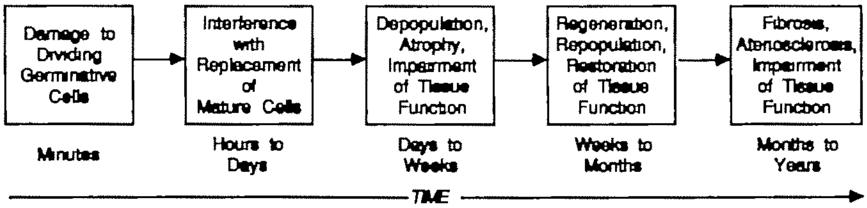

Damage to Dividing Germinative Cells
Interference with Replacement of Mature Cells
Depopulation, Atrophy, Impairment of Tissue Function
Regeneration, Repopulation, Restoration of Tissue Function
Fibrosis, Arteriosclerosis, Impairment of Tissue Function
Minutes
Hours to Days
Days to Weeks
Weeks to Months
Months to Years
TIME

FIG. 9.

Characteristic sequence of events in the pathogenesis of early and late non-stochastic effects of radiation.

whereas in the testis it takes several weeks (UNSCEAR, 1982).

The ability of a tissue to adapt to repeated exposures by increasing its output of differentiated cells also depends on its normal renewal kinetics. Tissues characterised by rapid cell turnover generally are better able to compensate, and thus withstand larger incremental daily doses, than do those with slow cell turnover (UNSCEAR, 1982).

Cell survival and proliferation

Because normal cell turnover depends on the proliferative integrity of the relevant precursor cells, that is, the ability of progenitor cells to proliferate and to form colonies of daughter cells, it is noteworthy that the acute dose required to deprive a proliferative cell of its reproductive capacity averages only 1–2 Gy of low-LET radiation (UNSCEAR, 1982). With high-LET irradiation, the fraction of cells retaining the ability to proliferate, *i.e.* "surviving" intact, typically decreases more steeply with dose, especially in the low-to-intermediate dose range (*e.g.* Fig. 10).

Cell survival curves such as those illustrated in Fig. 10 have been described by various mathematical models, the simplest being the expression:

$$S(D) = e^{-kD} \tag{3}$$

where $S(D)$ is the fraction of cells surviving after dose D, and k is a constant $= 1/D_0$ (UNSCEAR, 1982); however, this equation does not give the shoulder shown in curve E of Fig. 10, which can be represented by a multitarget, single-hit model of the form:

$$S(D) = e^{k_1 D}\left[1-(1-e^{-k_n D})^n\right] \tag{4}$$

where k_n is an expression of the sensitivity of each of n targets, all of which must be hit at least once to kill the cell. With this equation, the initial slope is given by $-k_1$, and the final slope by $-k_0$, where $k_0 = k_1 + k_n$.

To describe the continuously bending shoulder portion of the same dose–survival curve, the following model has been proposed:

$$S(D) = \exp-(\alpha D + \beta D^2) \tag{5}$$

where α and β are constants. According to this model, the cell can be killed either by a "single-hit" effect (expressed by the αD term) or by a "two-hit" effect (expressed by the βD^2 term) which results from the interaction of two intracellular sublesions neither of which is lethal by itself.

Because low-LET radiation is generally less effective per unit dose at low doses than at high doses, as indicated by the initial shoulder on the dose–survival curve (curve E of Fig. 10), and because successive doses of low-LET radiation separated by minutes or hours tend to be less than fully additive in their lethal effects, it is inferred that before cells lose their reproductive integrity, they are capable of accumulating a certain amount of sublethal damage, which is potentially reparable.

If the interval between successive exposures is long enough, the biological effectiveness of the radiation is likely to be reduced through the replacement of lethally injured cells as well as through the repair of sublethal damage (Fig. 11). The replacement of cells can occur through the regenerative proliferation of cells which survive irradiation or, in the case of a partially irradiated tissue, through the ingrowth of non-irradiated cells from neighbouring areas (Withers, 1969; UNSCEAR, 1982). The dose rate at which replacement and repopulation can counterbalance cell killing varies

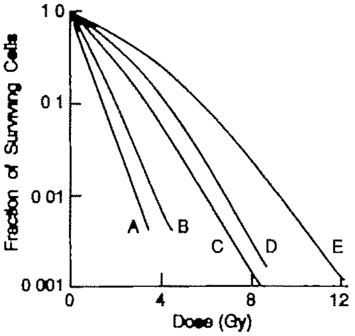


FIG. 10.

Human cell survival curves for exposure *in vitro* to radiations of differing LET (from Field, 1976).

Curve	Radiation		LET (keV/μm)
A	3.4–5 2	MeV α particles	86–140
B	8.3	MeV α particles	60.8
C	26.8	MeV α particles	24.6
D	6.3	MeV deuterons	11 0
E	200	kVp X rays	~2.5

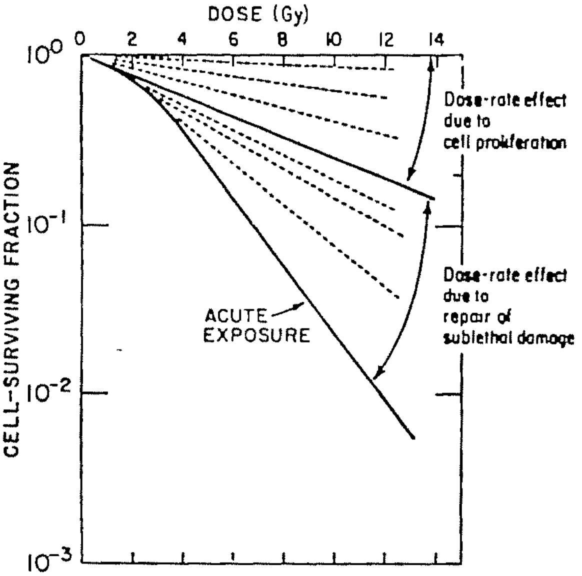


FIG. 11.

Illustration of the effects of repair of sublethal radiation damage and of cell proliferation on the population of cells surviving irradiation at different dose rates The dose–response curve for cells irradiated with X or γ rays in acute exposures (lower solid line) has a broad initial shoulder. As the dose rate is reduced, the slope of the survival curve becomes shallower and the extrapolation number tends towards unity, reflecting the repair of sublethal damage which takes place during the exposure. A limiting slope is reached (upper solid line), corresponding to complete repair of such damage If the dose rate is reduced further, below a critical value which varies with the cell cycle of the population exposed, cell proliferation may occur during irradiation, and there will be an additional dose-rate effect as the exposure is further protracted (modified from Hall, 1978)

among tissues, depending on their proliferative capacities.

With increasing LET, the initial slope of the dose–survival curve tends to become progressively steeper (Fig. 10) and the repair of intracellular damage to be reduced. As a result, the RBE of high-LET radiation generally increases with decreasing dose, dose rate and dose per fraction, reaching a constant value only at low doses or low dose rates (UNSCEAR, 1982).

The usual effect of fractionation, as indicated above, is to reduce the effectiveness of a given dose. Under certain conditions, however, it may actually enhance the effectiveness of a dose by causing cells in the surviving population to be redistributed into more radiosensitive stages of the cell cycle (UNSCEAR, 1982).

To characterise the severity of tissue damage in relation to LET, total dose, dose per exposure, number of exposures and overall duration of exposure, various mathematical models, or isoeffect formulae, have been proposed. Their applicability to exposures extending over many months or years is questionable, however, since the relevant information about dose–effect relationships has come largely from experience with radiation therapy regimens, which are characterised by relatively large doses fractionated over only a few weeks (UNSCEAR, 1982; ICRP, 1984). Most of our knowledge of non-stochastic effects, and hence the descriptions that follow, are based largely on such radiotherapeutic experience

Skin. Because of the superficial location of the skin, its reactions to radiation are known better than those of any other organ. The reactions vary in severity, depending on the depth and area of skin that are irradiated, as well as on the dose; furthermore, it is the dose to germinal cells in the basal layer of the epidermis that is critical (Cohen, 1966; Eads, 1972).

For erythema in a 10 cm^2 field, the threshold approximates to 6–8 Gy of X rays delivered in a brief exposure, or more than 30 Gy if the dose is delivered in highly fractionated exposures (UNSCEAR, 1982). To cause dry desquamation, moist desquamation or necrosis, higher doses are required, while the threshold for epilation is lower: 3–5 Gy of low-LET radiation in a single brief exposure can cause temporary epilation in some instances (UNSCEAR, 1982).

Epilation, desquamation and necrosis are attributed primarily to interference with epidermal cell renewal, and their timing corresponds to disturbances of cell turnover in the corresponding compartments of the epidermis (UNSCEAR, 1982). Late-occurring degenerative changes, on the other hand (*e.g.* atrophy and fibrosis), result in part from injury to dermal blood vessels (Law, 1981) as well as from injury to epidermal cells (Rubin, 1984). Microscopic changes in dermal capillaries, without other signs of injury to the skin, have been detected years after irradiation in atomic-bomb survivors exposed to doses in excess of 1 Gy (Tsuya et al, 1971), as well as in radiation workers exposed to 10–30 Gy of low-LET radiation over a period of 8–25 years (Leny et al, 1978)

Digestive system. The radiation response of the epithelium lining the mouth, pharynx, oesophagus and anus resembles that of the epidermis, while the epithelium lining the stomach, small intestine and colon reacts more quickly and tolerates less radiation in a single exposure. Large doses of radiation can kill enough germinative cells in the mucosal epithelium to interfere drastically with cell renewal in this tissue, causing ulceration and, ultimately, denudation of affected parts of the mucosa. Such effects can lead to a rapidly fatal dysentery-like syndrome if a substantial part of the small intestine is exposed acutely to more than 10 Gy (Hall, 1978). Localised injury from therapeutic exposure, on the other hand, may lead to such complications as fibrosis, stricture, intestinal perforation and fistula months or years later (Rubin & Casarett, 1968)

The liver, pancreas, and salivary glands are less radiosensitive than the gastrointestinal mucosa. Nevertheless, 30 Gy of conventionally fractionated therapeutic X radiation delivered to the entire liver may impair its function temporarily, and a larger dose can cause lethal hepatic failure (Kraut et al, 1972; Jeffrey et al, 1980). Such injury is not attributable to interference with the renewal of hepatocytes since the turnover of these cells is slow (UNSCEAR, 1982; ICRP, 1984). The salivary glands and pancreas are more radioresistant than the liver, but may undergo necrosis, atrophy, and fibrosis after 50–70 Gy of conventionally fractionated X irradiation (Rubin & Casarett, 1968; Cheng et al, 1981).

Haemopoietic system. Proliferating haemopoietic cells, which are among the most radiosensitive cells in the body, are killed in sufficient numbers by 2–5 Gy acute whole-body irradiation to cause fatal depression of the leukocyte and platelet counts within 3–6 weeks; however, a dose several times larger may be tolerated if the radiation is absorbed over a few months (UNSCEAR, 1982; ICRP, 1984). In pioneer radiologists, some of whom experienced severe depression of the blood count, the lifetime dose to the marrow is estimated to have averaged as much as 6.0 Gy (Marinelli, 1970). The threshold for detectable depression of haemopoiesis under the highly fractionated exposure conditions characteristic of occupational irradiation is estimated to exceed 0.4 Sv per year (ICRP, 1984).

Eye and other sensory organs. Damage to dividing cells in the anterior epithelium of the lens is observable microscopically in laboratory animals within minutes after acute exposure to 1 Gy (ICRP, 1984). The damaged cells and their breakdown products tend to accumulate eventually at the posterior pole of the lens, where they can produce dot-like subcapsular opacities. The opacities may not progress sufficiently to impair vision, depending on the dose of radiation (Merriam et al, 1972).

The threshold of low-LET radiation for opthalmologically detectable opacities has been estimated to be approximately 0.6–1.5 Gy in atomic-bomb survivors (Otake & Schull, 1982) and to range from about 2 Gy received in a single exposure to about 5.5 Gy received in fractionated exposures in radiotherapy patients (Merriam et al, 1972). In such patients, 5 Gy is the lowest dose observed to cause a progressive cataract (Merriam et al, 1972). With 7.5 MeV neutrons delivered in 12 fractions over 1 month, the threshold for a vision-impairing cataract has been estimated to be approximately 3–5 Gy (Roth et al, 1976), implying a neutron RBE of 2–3 under these conditions of exposure.

Occupationally induced cataracts have been observed after only 0.7–1.0 Gy of mixed neutron gamma radiation in early cyclotron physicists (Ham, 1953) and, more recently, in other radiation workers (Lvovskaya, 1974). In contrast, 1.5–4.0 Gy of low-LET occupational irradiation accumulated over a period of 10–20 years has not been observed to cause cataracts (Lvovskaya, 1974, 1976; Bendel et al, 1978).

Since the lens shows less sparing of injury on protraction of exposure than do other organs (Merriam et al, 1972), the threshold of protracted, occupational low-LET irradiation for a vision-impairing cataract is not expected to exceed 10 Gy, and may possibly be as low as 8 Gy (ICRP, 1984).

Other parts of the eye are comparatively radioresistant, as are other sensory organs (Rubin & Casarett, 1968).

Reproductive organs. Depending on their degree of maturation, the germ cells of the testis and ovary may be highly radiosensitive. Spermatogonia of intermediate maturity (Type A) are the most radiosensitive of germ cell stages in the testis. Enough such cells are killed by acute exposure to 0.15 Gy to curtail sperm production temporarily; and a dose in excess of 3–5 Gy, whether delivered acutely or fractionated over a few days or weeks, may cause permanent sterility (UNSCEAR, 1982). In dogs, exposure to only 6 mGy/day leads eventually to permanent sterility, whereas 1.2–1.7 mGy/day can be tolerated indefinitely without detectable effects on sperm production (Casarett & Eddy, 1968; Fedorova & Markelov, 1978, 1979).

In the human ovary, mature oocytes are the most radiosensitive of germ cell stages, being killed in sufficient numbers by acute exposure to 0.65–1.5 Gy to impair fertility temporarily; however, a dose of 6–20 Gy may be tolerated if fractionated appropriately (Lushbaugh & Ricks, 1972; Lushbaugh & Casarett, 1976). Because the ovary contains no pool of proliferating stem cells from which to replace its mature oocytes as they are lost through aging and ovulation, the threshold for permanent sterilisation of the ovary decreases with increasing age (UNSCEAR, 1982).

Central nervous system. The central nervous system is relatively radioresistant, although transitory electrophysiological changes can result from relatively small doses to the brain (UNSCEAR, 1982). Large doses can cause necrosis, demyelination, and vascular damage, leading to neurological symptoms and death within 1–3 years. The threshold for such effects is estimated at about 55 Gy delivered in 5.5 weeks to the whole brain (Sheline, 1980; UNSCEAR, 1982). Less severe changes have been observed in children many months after accidental or therapeutic irradiation in the dose range of 6–10 Gy (UNSCEAR, 1982; Ron et al, 1982).

The spinal cord is less resistant than the brain, undergoing demyelination, necrosis of neurons in the white matter and damage to the fine vasculature within 6 months to 2 years after a dose of 30 Gy delivered in 2 Gy fractions (Wigg et al, 1981; UNSCEAR, 1982).

Cardiovascular system. The heart is relatively radioresistant, but some degree of myocardial degeneration is likely to result from 40 Gy of conventionally fractionated therapeutic X radiation, and fatal pericarditis may result from a dose in excess of 60 Gy delivered to the entire heart (Stewart & Fajardo, 1972).

Blood vessels, in general, show changes after 40–60 Gy of conventionally fractionated X irradiation

(Law, 1981). These include increased vascular permeability, followed eventually by degeneration and sclerosis (Rubin & Casarett, 1968). Impairment of vascular function appears to be involved to some degree in the pathogenesis of most types of late radiation-induced tissue injury (Law, 1981; Rubin, 1984).

Urinary tract. A dose of 20–40 Gy fractionated over 3–4 weeks can impair renal function, and a larger dose may cause a fatal nephritis-like reaction within 6–12 months (Maier, 1972; UNSCEAR, 1982). The threshold for injury of the urinary bladder is higher: approximately 55–60 Gy fractionated over 4 weeks (Rubin & Casarett, 1968).

Respiratory system. Intensive irradiation of the lung may cause a pneumonitis within 2–6 months, which can be fatal if both lungs are exposed to more than 8 Gy in a single brief exposure or 20–30 Gy fractionated over 6–8 weeks (Fryer et al, 1978). A larger dose can be tolerated if delivered to only a small part of the lung (UNSCEAR, 1982). The nasopharynx, pharynx, larynx, trachea and bronchi are able to tolerate more than 30 Gy if the dose is delivered in 2 Gy fractions (Van den Brenk, 1971).

Musculoskeletal system. Although mature bone is relatively radioresistant, tolerating as much as 65 Gy fractionated over 6–8 weeks (UNSCEAR, 1982), retardation of bone growth may result from a dose of less than 1 Gy in children, depending on age at irradiation and the conditions of exposure (Tefft, 1972; Blot, 1975).

Mature cartilage, likewise, can tolerate more than 70 Gy fractionated over 10–12 weeks (Parker, 1972), and connective tissues show little response to radiation at doses below 50–60 Gy delivered in 2 Gy fractions (Rubin & Casarett, 1968)

Endocrine system. The endocrine glands are relatively radioresistant in normal adults, but they are less resistant in children. The threshold for marked depression of thyroid function in the normal adult is estimated to be approximately 25 Gy of conventionally fractionated X rays (Glatstein et al, 1971); however, lower doses may cause subclinical impairment of thyroid function. Thyroid function was severely depressed in a significant proportion of Marshall Islanders whose thyroids are estimated to have received 7–14 Gy from radioactive fallout in childhood; even among those who were more than 10 years old at the time of exposure, in whom the dose to the thyroid is estimated to have averaged slightly less than 4 Gy, four out of 45 later showed subclinical signs of decreased thyroid reserve (Larsen et al, 1982).

In comparison with the thyroid, other endocrine glands are more radioresistant. Permanent depression of pituitary and adrenal function is estimated to require approximately 45 Gy and 60 Gy, respectively, of conventionally fractionated therapeutic X irradiation (Rubin & Casarett, 1968; Einhorn & Einhorn, 1972, Samaan et al, 1982).

Implications for radiological protection. On the basis of radiotherapeutic experience, the tolerance of each organ for conventionally fractionated X or γ radiation delivered over a period of 4–7 weeks has gradually become known (*e.g.* Table III). No comparable tolerance, or threshold, values are known for more highly protracted exposure conditions, such as are characteristic of occupational irradiation. Nevertheless, it is likely that appreciably larger doses would be required to cause similar effects under the latter conditions (ICRP, 1984).

In considering the extent to which the currently recommended dose equivalent limits for radiation workers are compatible with the thresholds for non-stochastic effects, it must be borne in mind that 25 Sv is the largest dose that any organ could accumulate if irradiated selectively for 50 years at the occupational dose equivalent limit of 0.5 Sv/year and that, in practice, the dose would be restricted to a lower level by the dose equivalent limit for irradiation of the body as a whole (50 mSv per year) or by the relevant implied dose equivalent limit for stochastic effects (Table IV) It is noteworthy, therefore, that the only "threshold" values listed in Table III that are substantially lower than 25 Sv are those for the testes, ovaries, bone marrow, and lens of the eye.

With regard to the testes, available dose–response data imply that the testes of radiation workers could receive 1 mGy per day (or 0.3–0.4 Gy per year) indefinitely without detectable impairment of fertility (ICRP, 1984), from which it has been concluded that the existing implied stochastic dose equivalent limit for the testes (0 2 Sv per year) should suffice to protect against impairment of fertility in occupationally exposed men (Table IV). At the same time, it is recognised that if a worker's testes were to receive the annual dose equivalent limit (0.2 Sv) in a single brief exposure, his sperm count would probably be depressed temporarily.

The dose to the ovaries in a radiation worker is similarly limited in practice to the dose equivalent limit for the body as a whole (0.05 Sv per year), with the result that the maximum total dose that the ovaries are likely to accumulate in 50 years (2.5 Sv) is well below the estimated threshold for permanent sterility (6 Sv) (Table IV). Even in the unlikely event that the latter dose were to be reached after 30 years of occupational exposure at the implied stochastic dose equivalent limit for irradiation of the ovaries alone (0 2 Sv per year), the exposed woman would have reached the natural age of menopause by then.

For a vision-impairing cataract, the estimated threshold of protracted low-level occupational irradiation (> 8 Sv) (Table IV) exceeds the total dose that the lens could accumulate if exposed annually for 50 years at the currently recommended dose equivalent limit (0 15 Sv). Although, in principle, ophthalmologically detectable opacities might be produced under the latter unlikely circumstances, they would not be expected to be severe enough to impair vision

TABLE III

ESTIMATED THRESHOLD DOSES OF CONVENTIONALLY FRACTIONATED THERAPEUTIC X OR γ RADIATION FOR CLINICALLY SIGNIFICANT NON-STOCHASTIC EFFECTS IN ADULT PATIENTS*

Organ	Types of injury within 5 years after irradiation	Dose (Gy) causing effect		Area of irradiation field
		In 1–5% of patients	In 25–50% of patients	
Skin	Ulcer, severe fibrosis	55	70	100 cm^2
Oral mucosa	Ulcer, severe fibrosis	60	75	50 cm^2
Oesophagus	Ulcer, stricture	60	75	75 cm^2
Stomach	Ulcer, perforation	45	50	100 cm^2
Intestine	Ulcer, stricture	45	65	100 cm^2
Colon	Ulcer, stricture	45	65	100 cm^2
Rectum	Ulcer, stricture	55	80	100 cm^2
Salivary glands	Xerostomia	50	70	50 cm^2
Liver	Liver failure, ascites	35	45	whole
Kidney	Nephrosclerosis	23	28	whole
Urinary bladder	Ulcer, contracture	60	80	whole
Ureters	Stricture, obstruction	75	100	5–10 cm†
Testes	Permanent sterilisation	5–15	20	whole
Ovaries	Permanent sterilisation	2–3	6–12	whole
Uterus	Necrosis, perforation	<100	<200	whole
Vagina	Ulcer, fistula	90	<100	5 cm†
Breast	Atrophy and necrosis	< 50	<100	whole
Lung	Pneumonitis, fibrosis	40	60	lobe
Capillaries	Telangiectasis, sclerosis	50–60	70–100	—
Heart	Pericarditis, pancarditis	40	<100	whole
Bone	Necrosis, fracture	60	150	10 cm^2
Cartilage	Necrosis	60	100	whole
CNS (brain)	Necrosis	50	< 60	whole
Spinal cord	Necrosis, transection	50	< 60	5 cm^2
Eye	Panophthalmitis, haemorrhage	55	100	whole
Cornea	Keratitis	50	< 60	whole
Lens of the eye	Cataract	5	12	whole
Ear (inner)	Deafness	< 60		whole
Vestibulum auris	Meniere's	60	100	whole
Thyroid	Hypothyroidism	45	150	whole
Adrenal	Hypoadrenalism	< 60		whole
Pituitary	Hypopituitarism	45	200–300	whole
Muscle	Atrophy	<100		whole
Bone marrow	Hypoplasia	2	5.5	whole
Bone marrow	Hypoplasia	20	40–50	localised
Lymph nodes	Atrophy	35–45	< 70	—
Lymphatics	Sclerosis	50	< 80	—

*From Rubin and Casarett, 1972.

†Length, rather than area, irradiated

As far as the bone marrow is concerned, exposure of the haemopoietic system in its entirety is improbable except under conditions involving irradiation of the body as a whole. In practice, therefore, the dose equivalent to the marrow is usually limited to 0.05 Sv per year, which is well below the estimated threshold dose rate for detectable impairment of haemopoietic function (Table IV). The dose equivalent limit for stochastic effects in the marrow (0.4 Sv per year) is likewise below the estimated threshold for impairment of haemopoietic function (Table IV).

With respect to dose equivalent limits for high-LET radiation, a note of caution is warranted since the frequency and severity of non-stochastic effects decrease less on fractionation or protraction of exposure with high-LET irradiation than with low-LET irradiation. Because data on the non-stochastic effects of fractionated or protracted high-LET irradiation are relatively sparse, the magnitudes of the thresholds for such effects under occupational exposure conditions are highly uncertain. There is no evidence at this time that the relevant value of the quality factor, Q, needs to be

Cancer induction and non-stochastic effects

TABLE IV

ESTIMATED THRESHOLD DOSES FOR NON-STOCHASTIC EFFECTS IN ADULT HUMAN TESTES, OVARIES, LENS AND BONE MARROW*

Tissue and effect	Total dose equivalent (Sv)		Annual dose equivalent received as occupational irradiation (Sv)	Presently recommended annual dose equivalent limit (Sv)†	
	Received in a single brief exposure	Received in highly fractionated or protracted exposures		if tissues irradiated alone	if tissues irradiated with the whole body
Testes:					
temporary sterility	0.15	NA‡	0.4	0.2	0.05
permanent sterility	3.5	NA	2.0	0.2	0.05
Ovaries: sterility	2.5–6.0	6.0	>0.2	0.2	0.05
Lens					
detectable opacities	0.5–2.0	5	>0.1	(0.15)	0.05
visual impairment (cataract)	5.0	>8	>0.15	(0.15)	0.05
Bone marrow§					
depression of haemopoeisis	0.5	NA	>0.4	0.4	0.05
fatal aplasia	1.5	NA	>1	0.4	0.05

*From ICRP, 1984.

†Values listed, except those in parentheses, denote implied annual dose equivalent limits for stochastic effects, which are limiting for the tissues in question

‡NA denotes not applicable, since the threshold is dependent on the dose rate rather than on the total dose.

§Dose equivalents listed are values averaged over the entire marrow.

increased, but the question merits continuing review (ICRP, 1984).

Susceptibility to some non-stochastic effects (impairment in the growth of cartilage and bone, for example) is appreciably higher in children than in adults, from which it follows that the corresponding exposure limits should be lower for the general public than for radiation workers. It is noteworthy, therefore, that the exposure limits for stochastic effects for members of the public are 10 times lower than those for radiation workers (*e.g.* than the values tabulated in the last column of Table IV). Hence, they should suffice to protect adequately against non-stochastic effects in the general population (ICRP, 1984).

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Hereditary effects of radiation: some evidence from animal experiments

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Abstract

Data on hereditary effects of radiation in man remain very limited, and hence estimation of genetic hazards is based largely on results from animals.

In males, extensive work on gene mutations and chromosome aberrations has shown that not only reduction of dose rate but also fractionation of the dose can reduce the mutational yield, and such effects may be due to changes in the cell population structure with prolonged or repeated treatment In female mice the dose–response relationship for gene mutation is curved, probably due to the effects of DNA repair. Mouse primary oocytes, which receive the major part of the lifetime dose, are very insensitive to mutation by radiation, but it is not yet known whether all species are equally insensitive

A major part of the incidence of genetic disease in man is due to conditions of complex or irregular inheritance, such as congenital malformations. There has been doubt whether the incidence of such diseases would be altered by a change in mutation rate. It is now known that the frequency of congenital malformations among the offspring is increased by irradiation of either male or female mice before conception and the effect can be transmitted to the second generation. However, the increases are relatively small

Similarly, until recently there has been doubt whether chromosomal non-disjunction (which in man is a cause of Down's syndrome) was increased by irradiation. Dose–response curves for the induction of non-disjunction in mature or growing oocytes of mice have now been obtained. However, the work involved relatively high doses and sensitive stages. The effects of low dose rates, and in primary oocytes, remain to be investigated.

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Irradiation of the embryo and fetus

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ABSTRACT

The human evidence on radiation damage to the individual developing *in utero* is confined to mental impairment and carcinogenesis. New evidence is becoming available about levels of mental impairment of direct interest to radiological protection, but as yet no framework of understanding exists to allow quantitative predictions for the purposes of radiological protection There is general agreement that malignant disease has been increased following antenatal radiography but no unanimity yet in concluding that irradiation was the main causal factor. reasons are given for accepting that radiography was the cause. Recent increases in biological understanding suggest why maldevelopment is not to be expected after irradiation of the conceptus. A clonal hypothesis for organogenesis provides a reasonable explanation for quantitative aspects of experimental observations on teratogenesis by ionising radiation, including the commonly found highly curvilinear dose–response relationship, the occurrence of so-called critical stages of sensitivity after exposures of a few hundred roentgens, and the reduction in frequency of induced abnormality with protraction of exposure. Clonal hypotheses predict that there will be a virtual threshold for polycytic (non-stochastic) forms of radiation damage. It may be misguided to adopt a linear dose–response relationship for deriving risk estimates for the practical purposes of radiological protection unless some mechanism for production of clinically evident harm can be advanced which provides a plausible reason for expecting linearity

The developing individual *in utero* has occupied a special niche in radiological protection for more than a quarter of a century. "The safest procedure is to restrict pelvic irradiation, whenever possible, to the two weeks following the onset of menstruation" (Russell & Russell, 1952). This proposal was based on the belief that the conceptus before implantation was especially vulnerable. It became formally one of the Recommendations of the International Commission for Radiological Protection (ICRP, 1966, Para 76), commonly but erroneously called the 10-day rule The recommended 10-day option was in terms of 10 days rather than 2 weeks to allow for the differences between individual women in the day of ovulation after onset of the previous menstrual bleeding. However, there never was sound evidence that the pre-implantation conceptus was especially vulnerable to induction of malformations and, recently, the categorical statement was made by one of the authors cited above that "irradiation during the (roughly) 9-day preimplantation period is virtually without risk of abnormality in a surviving child" (Russell, 1980).

OBSERVED DAMAGE IN THE HUMAN FOLLOWING EXPOSURE *IN UTERO* TO IONISING RADIATION

No observations have been reported on the effect of irradiation during the first fortnight after conception.

During the 1920s, abdominal irradiation of the mother was strongly recommended by some obstetricians and radiologists as a convenient, efficient and relatively non-toxic means of therapeutic abortion. It seemed to have a special value in women with severe pulmonary tuberculosis, in whom pregnancy could be disastrous, since irradiation avoided surgery and anaesthesia by inhalation (the only method then available). However, when irradiation failed, live-born children were sometimes found to have severe mental retardation in childhood or adolescence. More severe cases were clearly microcephalic at birth or after a few months of post-natal development. When X irradiation or radium in the cervix was used to treat cases of carcinoma of the cervix or uterine fibroids without preliminary curettage (which became the rule only later), similarly affected children were also sometimes born. About 100 case reports can be found in the literature, in many of which mental retardation was the only abnormality noted. The doses involved are mostly unknown but must often have been in the therapeutic range for cancer. There is no possibility of estimating the frequency of risk per unit dose. There is a remarkable lack of published information on the structure of the abnormal brains

Many years later, severe mental retardation has become the most important damaging consequence following pre-natal exposure to the atomic bombs in Japan (Table I) but, in contrast, malformations and malignant disease have not been seen in excess. Perinatal mortality was increased only after exposure in the third trimester and after large maternal exposures, from just sublethal upwards.

After abdominal or pelvic radiography of pregnant women, it has been clearly established that the childhood cancer rate in their offspring is higher than in those who were not irradiated *in utero*. What is still under discussion is the cause of the excess.

For the purposes of radiological protection the human evidence is too limited in scope and must be supplemented by consideration of animal experiments, even though these may seem to contradict human

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TABLE I

SEQUELAE OF PRE-NATAL EXPOSURE TO ATOMIC-BOMB RADIATION (MOLE, 1984)

Neonatal (perinatal) mortality	Increased only after exposure in the third trimester and when maternal exposure (kerma) > 180 cGy T65D (Kato, 1971)
Congenital malformations (including Down's syndrome)	No excess recorded
Death from malignant disease at 0–24 years of age[*]	Three deaths recorded: about two expected (Kato, 1971)[†]
Severe mental retardation	Only with exposure at 10–27 weeks after LMP (Otake & Schull, 1983, 1984)
Infertility	No relationship of level of exposure to frequency of childless marriage, number of births in marriage, or interval between marriage and first birth (Blot et al, 1975)

LMP = last menstrual period.

[*] Surviving beyond the first birthday: 453 subjects > 10 cGy T65D, 735 subjects < 10 cGy T65D.

[†] Follow-up until 1976 (30–31 years after exposure *in utero*) showed five deaths from malignant disease (two leukaemia, one stomach, one liver, one large intestine) but no increase in overall frequency with increase in dose and no excess (Kato, 1978).

experience. A great variety of malformations has been found after experimental irradiation at the embryonic stage of development, as compared with virtually none in the human; conversely, animal experiments have consistently failed to show an increase in malignant disease after intrauterine irradiation.

THE NECESSITY FOR EXTRAPOLATION BEYOND THE OBSERVATIONS

For the purposes of radiological protection, estimates of risk from tissue doses of 10 mGy (1 rad) or less are required and, apart, perhaps, from malignant disease in man, such estimates will have to be derived by extrapolation since all the other evidence both in man and in animals comes from larger or much larger tissue doses. Extrapolations from larger doses to smaller doses are valid only if they are based on a sufficient understanding of the biological characteristics of the different stages of intrauterine development and of the radiobiological implications of radiation dose at the cellular and tissue level. That means considering the whole organism, not simply cells in isolation. As more is learnt, it seems to me to be increasingly misguided to adopt a linear dose–response relationship when deriving risk estimates for the practical purposes of radiation protection, unless some mechanism for production of clinically evident damage can be advanced which provides a plausible reason for expecting linearity at the dose levels where such damage is observed. Extrapolations from animals to man involve further considerations.

HUMAN EVIDENCE ABOUT RADIATION DAMAGE FOLLOWING INTRAUTERINE IRRADIATION

Quantitative observations on the fetus and brain damage

Quantitative information on mental impairment in relation to dose and to the significance of the timing of radiation exposure in relation to gestational age comes from Japanese atomic-bomb survivors (Otake & Schull, 1983). Severe mental retardation (SMR) was not found in these people after exposure at 0–7 weeks post-conception (p.c.); most cases of SMR occurred after exposure at 8–15 weeks p.c., with fewer cases at 16–24 weeks p.c. and there was no excess at 25+ weeks p.c. (Otake & Schull, 1983). The period of maximum sensitivity corresponds very closely to the range of gestational ages over which the primitive forebrain develops in man and during which the DNA content of the forebrain increases logarithmically (Dobbing & Sands, 1973; Mole, 1982). Most neuroblast cell division in the primitive forebrain is programmed to cease at about the 16th week p.c.

The timing of the period of greatest sensitivity seems to fit well with the accepted generalisation that populations of cells in cell division are relatively radiosensitive. The sensitivity of brain function in man to radiation damage is in line with extensive observations in animals on the specific radiosensitivity of neuroblasts to intermitotic death by nuclear necrosis. Observations on the forebrains of two aborted fetuses exposed to Ra γ rays 2 and 6 days previously have confirmed that human neuroblasts are similarly sensitive (Driscoll et al, 1963). Other aspects of normal development, such as the migration of primitive neurons from their place of birth (in or near the roof of the ventricle as a result of neuroblast cell division) and the development of interconnections between neurons, may also be processes sensitive to radiation damage. There is a great deal more to learn. The dose–response for the reported data on frequency of severe mental retardation in individuals irradiated *in utero* during the period of maximum sensitivity is strikingly linear with dose (Otake & Schull, 1983; Schull et al, 1986).

Observations on lesser degrees of mental impairment are now becoming available. The grades of performance of children at school in Japan are systematically recorded by the teachers according to standardised criteria. Records for 1955–56 were abstracted for subjects exposed *in utero* and selected as a defined population for continued follow-up. For each of seven different school subjects the performance grade was clearly related to dose in those exposed at the sensitive gestational age range, 8–15 weeks, but not in those exposed at the insensitive gestational ages, 0–7 and 25+ weeks (Table II, adapted from Schull and Otake, 1986). Those exposed at 16–24 weeks showed an intermediate picture.

TABLE II

DEPENDENCE OF PERFORMANCE IN FIRST GRADE OF SCHOOL ON FETAL TISSUE DOSE IN ATOMIC-BOMB SURVIVORS EXPOSED *IN UTERO*, ACCORDING TO GESTATIONAL AGE AT EXPOSURE (ADAPTED FROM SCHULL AND OTAKE, 1986)

School subject	Linear regression of performance score on fetal tissue dose					
	Statistical significance of coefficient*; post-conceptional age (weeks) at exposure:				Coefficient for 8–15 weeks $\times 10^3$	
	0–7	8–15	16–25	25+	mean	SE
Japanese	Nil	0.001	0.005	Nil	18	4
Mathematics	Nil	0.001	0.001	Nil	18	4
Science	Nil	0.001	0.001	Nil	17	4
Civics	Nil	0.001	0.01	Nil	16	4
Drawing, handicraft	Nil	0.001	Nil	Nil	16	4
Music	Nil	0.001	0.05	Nil	12	4
Gymnastics	Nil	0.001	0.05	Nil	11	3

Age on first starting school c.6 years Routine grading by teachers in five steps (−2 to +2) arranged so that 5%, 20%, 50%, 20% and 5% of the children in a class would fall into successive categories. A few children classed as severely mentally retarded in other specific investigations not connected with schooling were, in fact, at ordinary school and so are included in the school population on which these analyses are based.

*p values in discrete steps, nil indicating > 0.05

TABLE III

SEVERE MENTAL RETARDATION IN JAPANESE ATOMIC-BOMB SURVIVORS EXPOSED *IN UTERO* SELECTED DATA FROM OTAKE AND SCHULL (1983) AND SCHULL AND OTAKE (1986)*

	Gestational age (post-ovulatory)							
	Irradiation at 8–15 weeks inclusive							All gestational ages
Range of fetal tissue dose (cGy)†	<1	1–9	10–49	50–99	100–199	200+	Grouped 100+	<1
Hiroshima								
No of subjects	210	65	38	11	3	1	4	832
Severe mental retardation, all cases	0	3	4 (a)	4 (b)	3	0	3	5 (c,d)
Without "significant clinical findings"‡	0	3	2	3	3	0	3	3
Group mean fetal tissue dose (cGy)†	0	4	23	72	137	438	212§	0
Nagasaki								
No. of subjects	47	4	12	2	3	2	5	253
Severe mental retardation, all cases	2	0	0	0	2 (e)	1	3	4 (f,g)
Without "significant clinical findings"‡	2	0	0	0	1	1	2	2
Group mean fetal tissue dose (cGy)†	0	7	22	71	126	219	163§	0

*The corresponding data in Otake and Schull (1984) require correction (Schull & Otake, 1986)

†Fetal dose inferred from maternal kerma T65DR plus ORNL factors for attenuation The group mean values are based on all gestational ages (At Hiroshima over all gestational ages there was only a single subject in the 200+ cGy group· that shown in the table.)

‡"Significant clinical findings" in the excluded subjects provide reasons for inferring that irradiation was not the primary cause of their severe mental retardation (a) Down's syndrome, two cases (b) neonatal jaundice, (c) Down's syndrome, (d) retarded sibling, (e) neurofibromatosis, (f) "possible birth trauma" (interpreted as definite trauma possibly damaging the brain), (g) congenital lues (syphilis). A ninth subject exposed at 20 weeks of gestation suffered from Japanese B encephalitis at 4 years of age. The definitive diagnoses of severe mental retardation were made at about 17 years of age (or earlier). Fortunately, the two cases (d) and (f), where "significant clinical findings" might seem inadequate to justify exclusion, are both zero-dose cases and how they are dealt with is virtually immaterial to the results in Table IV

§Average of city-specific group mean fetal tissue dose for the two highest dose groups, weighted according to the number of subjects in a dose group

TABLE IV

REGRESSION OF SEVERE MENTAL RETARDATION ON FETAL TISSUE DOSE IN SUBJECTS EXPOSED *IN UTERO* AT 8–15 WEEKS POST-OVULATORY AGE (PRIMARY DATA IN TABLE III)

Regression equation	Highest two dose groups	Zero dose frequency specific for		All cases*			Cases without significant clinical findings*		
		age of gestation	city	% SMR at zero dose, mean†‡	Regression common to both cities, mean (SE) 10^{-2} Gy^{-1}	*p* for fit§	% SMR at zero dose, mean (SE)†¶	Regression common to both cities, mean (SE) 10^{-2} Gy^{-1}	*p* for fit§
Linear ($y = c+bD$): cities kept separate in each calculation**					*b*			*b*	
	Grouped	+	+	H = 0; N = 4.3	38 (6)	0.3	H = −0.2; N = 2.9	33 (8)	0.1
	Grouped	−	−	0.83	37 (6)	0.8	0.50 (0.22)	30 (7)	0.6
	Not grouped	+	+	H = 0, N = 4.3	21 (4)	0.000 008	H = +0.4, N = 3.1	19 (5)	0.003‖
	Not grouped	−	−	0.83	20 (4)	0.0006	0.54 (0.23)	19 (5)	0.009‖
Quantal ($y = c+(1-c)\exp-aD^n$) cities kept separate in each calculation**					*a*			*a*	
	n taken = 1								
	Grouped	+	+	H = 0; N = 4.3	53 (13)	0.6	H = −0.9; N = 3.0	47 (16)††	0.08
	Grouped	−	−	0.83	50 (13)	0.8	0.49 (0.21)	36 (11)	0.6
	Not grouped	+	+	H = 0; N = 4.3	51 (18)	0.04	H = −0.7; N = 3.0	44 (23)‡‡	0.01‖
	Not grouped	−	−	0.83	47 (12)	0.1	0.49 (0.22)	35 (10)	0.1

When $n > 1$ the dose response is sigmoid but, when n is estimated, the data are too scanty to give statistically established values of a. For cases without "significant clinical findings" using pooled controls and with and without grouping of the two highest dose groups, the values of a are 53(±62) and 100(±90) at Hiroshima as compared with 0.01 or smaller (±62 or ±160) at Nagasaki. The corresponding values of n are 1.0(±0.3) and 0.8(±0.2) at Hiroshima and 13(±18) and 2.4(±1.6) at Nagasaki. A value of $n = 2$ implies a dose-squared response.

The statistical calculations were made by D. H. Papworth (personal communication).

*Table III gives the group mean doses and the "significant clinical findings" in the excluded subjects.

†H = Hiroshima, N = Nagasaki.

‡The frequency observed at zero dose was taken as given

§*p* values for fit are far from satisfactory as a guide to adequacy of fit when the numbers of cases per cell are as small as in Table III.

¶The frequency at zero dose was estimated

‖SE of mean regression slope increased by the factor for heterogeneity.

**Except that zero dose frequency not specific for age of gestation was the pooled value for both cities, as well as for all ages of gestation.

††Difference in slope between cities by log likelihood ratio, $p = 0.032$ (H = 84%, N = 17% per Gy).

‡‡Difference in slope between cities by log likelihood ratio, $p = 0.059$ (H = 70%, N = 17% per Gy)

Schull and Otake (1986) emphasised the limitations on interpretation of the findings. The seven different sets of gradings cannot be regarded as independent of each other: a child with an above-average grade for, say, Japanese, is more likely than not to have an above-average grade for mathematics, science etc., and conversely. Moreover, the data in Table II come from a preliminary analysis of as yet incompletely collected information and detailed consideration has yet to be given to other factors which might have some bearing on the correlations (*e.g.* first-cousin marriages among parents, infective illnesses in the children, nutritional deficiency and indirect influences via radiation damage in the mothers of the children). Nevertheless, the findings reported in Table II are striking. Intelligence tests are also available from 1955–56 and the scores for those exposed at 8–15 weeks of gestation are quantitatively related to fetal doses with or without the inclusion of those diagnosed clinically as having SMR (Schull & Otake, 1985). Much more information on these and other obervations is to be expected in the next few years.

Application of the findings for the purposes of radiological protection

The quantitative evidence available so far comes from atomic-bomb survivors who received a brief exposure, lasting less than a minute. Critical issues in applying the available information are the degree of amelioration of damage when radiation exposure is protracted and the principles for deriving from large exposures a risk estimate appropriate for exposures at occupational dose limits and below.

In ordinary circumstances a definite cause cannot be assigned to most cases of severe mental retardation. When considering atomic-bomb survivors, there is an important distinction between cases of mental retardation with a medical diagnosis suggesting a definite cause unrelated to irradiation and cases without such a suggested cause and which, therefore, could have been caused by radiation. The causes implied by "significant clinical findings" are listed in Table III.

Dose–response relationships. Alternative dose–responses for severe mental retardation have been derived, including and excluding cases with "significant clinical findings", *i.e.* with a presumptive primary, medically defined cause other than radiation. Table III provides the basic information; Table IV gives the results. The dose–responses for all cases and for cases without "significant clinical findings" were not distinguishable. With a fitted simple linear dose–response there was no statistically established difference between Hiroshima and Nagasaki, and the risk coefficient, b, was twice as large when the two highest dose groups were grouped together before analysis than when they were kept separate (Table IV).

The fitted linear regressions treat SMR as if it was a stochastic phenomenon. Mental retardation can vary greatly in degree but the grade of severity was not a variable in the calculation: each individual either had SMR or did not. It is commonly supposed that a stochastic response will be linear with dose but this is not so over the whole range of response up to 100%. The frequency of "no effect" y for dose D varies according to $\exp(-\lambda D)$ and $-\log y$ is linear with D. The frequency of "presence of effect" $(1-y)$ varies according to $[1-\exp(-\lambda D)]$. This is very nearly linear with D over the effect range 0–2% but diverges increasingly from linearity with increase in response towards 100% (which will be reached only asymptotically) (Fig. 1). Thus, the good fit of such high levels of response as 30–75% SMR to a simple linear function $(c+bD)$ (Otake & Schull, 1983; Schull et al, 1986) may suggest that a stochastic framework is not an appropriate framework for quantitation. Paradoxically, perhaps, the better the fit to linearity in a statistical sense at high levels of response, the stronger is this conclusion. It is independent of biological mechanism and depends simply on the stochastic classification of SMR as present or absent. In any case, the apparent goodness of fit of linearity to the observations on SMR depends critically on whether the two highest dose groups are pooled for the analysis (Table IV).

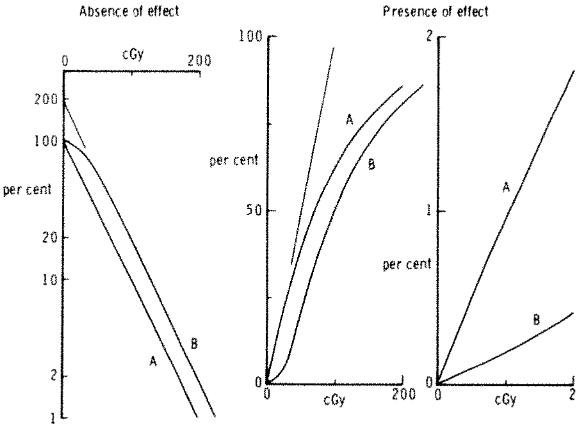

FIG. 1.

A stochastic dose–response relationship to illustrate the difference between "absence of effect" and "presence of effect". Curves A are for log $y = e^{-\lambda D}$ for absence of effect and for $y = (1-e^{-\lambda D})$ for presence of effect, λ being given the value 0.01 cGy^{-1}. Curve B has a shoulder on the $e^{-\lambda D}$ plot for absence of effect and the curves B on the other two plots show how this shoulder translates into presence of effect. The extreme right-hand plot illustrates the difference between A and B for presence of effect in the dose region of interest to radiological protection, 0–2 cGy.

A radiobiologically standard stochastic response is given by $y = c+(1-c)[1-\exp(-aD^n)]$, simplifying to $(c+aD^n)$ at low doses when $c \ll 1$. With $n = 1$, the coefficient a at low doses is 1.5–2.5 times larger than the linear coefficient b but with larger standard errors. There is arguable evidence that results from Hiroshima

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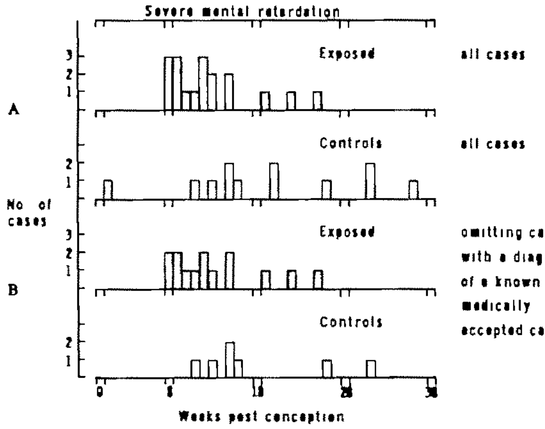

FIG. 2

Distribution of cases of severe mental retardation in Japanese bomb survivors exposed *in utero*, according to age post-conception (weeks) at the date of the atomic-bomb explosions (Hiroshima and Nagasaki combined) (from Mole, 1986) Fetal tissue dose using Kerr's ORNL shielding factors. Controls < 5 rad T65DR, exposed 6–229 rad T65DR. The upper two panels include all cases The lower two panels exclude all the cases with a medical diagnosis suggesting a cause for the severe mental retardation: five of the 12 control cases and four of the 18 exposed (clinical details in Table III)

and Nagasaki may differ quantitatively (Table IV footnote)

Severe mental retardation would appear to be a non-stochastic form of radiation damage since mental impairment is undoubtedly graded in severity. But so is a functional defect in any irradiated organ and no difficulty seems to arise, for example in relation to thyroid function and radiological protection, in accepting a threshold level of protracted exposure for non-stochastic effects and in basing a quantitative statement of the threshold on clinical experience. However, there is a natural reluctance to take the same attitude where mental impairment is concerned.

The risk coefficients in Table IV refer to a level of damage to organ function well in excess of that acceptable when considering non-stochastic effects in general. They are subject to change when the current revision of dosimetry in Japanese bomb survivors is completed. In few cases of SMR could irradiation be the sole cause (Table III) and the risk coefficients depend critically on a total of only some 20 individuals at the higher levels of exposure. If fetal tissue dose was changed in only one or two of them, risk coefficient values could change markedly, especially when calculated using simple linearity.

It is conceivable that degree of impairment of post-natal mental function (but surely *not* frequency of SMR) is related to the number of neuroblasts lost, however small, during the early fetal stage at 8–15 weeks p.c. when the primitive forebrain is being constructed. Such a hypothesis might justify a stochastic framework for predicting detriment at low levels of radiation exposure *in utero*. Possibly the most important quantitative factor then would be whether there is a shoulder in the relationship between inactivation of neuroblasts and radiation dose and how large it is. As shown by the curves labelled B in Fig. 1, this would be a major determinant of the magnitude of risk at doses in the range 0–2 cGy. But there seems little purpose in discussion of an appropriate framework for prediction in the abstract and without considering possible biological mechanisms for the causation of SMR and/or smaller degrees of impairment of mental function by low levels of radiation exposure.

Was radiation the only factor responsible for severe mental retardation in bomb survivors without "clinically significant findings"? Figure 2A shows the distribution of all the cases of SMR according to gestational age on the day of exposure to bomb radiation; Fig. 2B the corresponding distribution of cases without "clinically significant findings". In Fig. 2A the control cases seem to be distributed at random across the whole range of gestational ages, as expected because they were not irradiated. Most of the irradiated cases were exposed over the period 8–15 weeks p.c., as, again, expected because the developing forebrain at that stage of pregnancy would be specifically radiosensitive. However, when all the cases with a presumptive primary medically defined cause other than irradiation are omitted, as in Fig. 2B, the control cases seem to be concentrated over the same limited range of gestational ages as the irradiated cases. The excess in the irradiated group is undoubted (the number of subjects at risk was much smaller than for controls, Table III), but it is no longer self-evident that it was necessarily only irradiation and irradiation at 8–15 weeks p.c. which caused that excess. Was there some factor other than radiation which, over a limited calendar period, caused SMR to occur in some of those who escaped irradiation? If so, it is not clear whether the excess in the irradiated without "clinically significant findings" was caused by their irradiation alone or by the combined action of both factors. In principle, this could make a quantitatively large difference to inferences by extrapolation about the likely effect of irradiation *in utero* by exposures leading to fetal doses of 1–10 mGy.

Carcinogenesis

The first reports of an excess mortality from malignant disease in children who had been exposed *in utero* to diagnostic radiography were by Stewart et al (1956, 1958). The pooled results of many subsequent surveys confirmed this pioneer finding (MacMahon & Hutchison 1964; Committee on the Biological Effects of Ionising Radiation (BEIR), 1980; Doll, 1981, MacMahon, 1985). Because the excess rate in the pooled data is low, about one cancer death in 4000–5000 exposed children, it is to be expected that no excess would be demonstrable in a number of the individual surveys, especially those reviewing the smaller numbers of subjects, and also that, often, the excess risk in a particular survey would not exceed limits set by statistical chance. Recent additional surveys have shown the same picture. Statistically non-significant excesses associated with radiation exposure were found in the USA (Shiono et al, 1980) and in Finland (Salonen, 1976). A statistically acceptable increase in relative risk was found in a case-control study in the USA of cancer mortality of twins (Harvey et al, 1985) and, for the first time, in a study of incidence of (rather than mortality from) malignant disease. Preliminary results from a UK study of incidence showed a positive association with some specific categories of malignant disease but not for all cancers taken together (Hopton et al, 1985) However, an extension of the large and most carefully controlled USA study (Monson & MacMahon, 1984), while confirming the magnitude of the excess rate for leukaemia, found a smaller excess rate of other cancers than that reported earlier.

Most reviews of the field agree that there is an excess cancer mortality in childhood associated with previous exposure to diagnostic irradiation *in utero* (BEIR, 1980; Doll, 1981, MacMahon, 1985). They disagree about the relative weight to be attached to two possible explanatory hypotheses for the observed correlation, that radiography was itself the "direct cause" or, alternatively, that selection for maternal radiography in pregnancy was simultaneously selection for children who were destined to have a higher frequency of malignant disease in childhood than average. What may be termed the "selection hypothesis" is logically a compound hypothesis, that there will be reasons for selecting some pregnant women for X-ray examination rather than others (a wholly acceptable proposition) and that those reasons are predictive of a higher cancer rate in childhood than average. No *a priori* or independent reasons have been put forward in favour of this second part of the compound hypothesis: it may seem purely *ad hoc* and proposed to avoid accepting the "directly causal" hypothesis because this is thought to be intrinsically unlikely. Certainly, the "directly causal" hypothesis, if accepted, seems as good evidence as could be found for the idea that there is no threshold dose for carcinogenesis by ionising radiation, a concept strenuously resisted by some for strictly scientific reasons and by others rather more pragmatically. In fact, the two hypotheses are not mutually exclusive: both could be true. Stating a preference for one does not entitle someone to discard the other and finding evidence for the one will never disprove the other.

The quantitative similarity of fetal and post-natal radiosensitivity. A serious and prolonged search for the postulated selective factor (or factors) has failed to uncover any (Doll, 1981; MacMahon, 1985) and there seems to be no compelling reason for maintaining that it must exist. There is nothing unexpected or defective about the "directly causal" hypothesis. The experience of Japanese atomic-bomb survivors during the 35 years after post-natal irradiation gives an overall risk for induction of fatal malignant disease by uniform brief whole-body exposure in the range $1–2\times10^{-2}\ \mathrm{Gy}^{-1}$ T65D kerma (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1977a; BEIR, 1980). A closely similar risk rate of $2–2.5\times10^{-2}\ \mathrm{Gy}^{-1}$ fetal tissue dose is stated by UNSCEAR (1972, 1977a) for whole-body exposure *in utero* based on observations over the first 10 years of life. This is not likely to be a serious underestimate of the lifetime risk after *in-utero* exposure because the excess in childhood cancer mortality seems to be largely, though not wholly, confined to the first 10 years of life Moreover, a shorter average latent period for cancer induced by pre-natal than by post-natal irradiation would seem to be biologically likely. Thus, on the "directly causal" hypothesis, the risk for cancer induction by very brief radiation exposures is numerically similar both in atomic-bomb survivors of all ages and in those exposed to radiography *in utero*, as judged by linear risk coefficients derived in a conventional manner. If so, there is surely no fundamental barrier preventing acceptance of diagnostic radiography of the fetus as a cause of cancer. Accepting the "causal hypothesis" does not involve accepting a supersensitivity of the fetus as has been supposed (Monson & MacMahon, 1984; BEIR, 1980, p. 442).

It does not seem necessary to consider post-natal irradiation, as in intensive care of low-birth-weight neonates, as a potentially misleading factor (Harvey & Boice, 1985). Multiple diagnostic X-ray examinations in such circumstances were rarely used 30 years ago when most of the children in the various surveys were born. Also, post-natal X-ray exposures are to only a part of the body and the tissue dose per examination for a neonate is much smaller than the corresponding dose in a fetus within the body of its mother (full details in Fletcher et al, 1986).

Arguments for and against a "directly causal" hypothesis. A main reason offered against accepting the "directly causal" hypothesis is that the small population of atomic-bomb survivors exposed *in utero* has not shown the expected increase in incidence of childhood cancer. A rate of $2\times10^{-2}\ \mathrm{Gy}^{-1}$ leads to an expectation of 3–4 excess cancers in 500 individuals receiving an average fetal tissue dose of 0.3–0.4 Gy. (There were 453 subjects with maternal kerma in the range 10–499 rad and mean 60–70 rad, the fetal tissue dose being about 0.5 × kerma; Table II in Mole, 1974.) It is now generally recognised that an expectation for number of induced cancers derived by applying a linear regression coefficient to a range of dose rising to several grays will be unrealistically high (Mole, 1975; UNSCEAR, 1977a; BEIR, 1980) Applying the necessary radiobiologically based corrections reduced the expected cancers in atomic-bomb survivors exposed *in utero* by a factor of 2–4 (Mole, 1974), that is, from 3–4 to 1–2 cases. Thus, a clear excess of induced cancer is not to be expected in the available sample of bomb survivors exposed *in utero* and the absence of an excess is not a reason for denying the "directly causal" hypothesis as the explanation for the excess cancer in childhood associated with maternal diagnostic radiography. The current revision of the bomb-survivor dosimetry seems unlikely to weaken seriously the force of this conclusion.

There is, in fact, a positive argument in favour of the "directly causal" hypothesis. In the Oxford Childhood Cancer Survey (OCSS), twins *in utero* were exposed to maternal radiography 5–6 times more frequently than singleton births. When singletons, monozygotic (identical) (MZ) twins, and dizygotic (unlike) (DZ) twins were distinguished and leukaemias and all other cancers were examined separately, there were six comparisons, each showing a rate of malignant disease in the irradiated in excess of that in the unirradiated group (Table V). The excess rates in singleton births and DZ twins were closely similar; those for MZ twins less comparable. The chance probability that six comparisons will all be in the same direction is $2^{-6} = 0.016$.

The evidence from DZ twins must also minimise the quantitative significance of the unknown selective factor which has been postulated as predicting more cancer in the children of pregnant women selected for radiography than other children. Genetic diversity in singletons and DZ twins should be broadly similar. Because the radiography rate was 5–6 times higher in twins than in singletons, the excess rate associated with radiography and attributable to this unknown factor should be much smaller in DZ twins than in singletons, perhaps only about one-fifth of the excess in singletons The observations (Table V) do not conform to this expectation: the excess rate in DZ twins was the same as in singletons. Indeed, no quantitative predictions seem to have been published stating what differences in excess cancer between singletons and twins would be expected according to the "selection hypothesis".

The argument has also been used that, because twins are exposed to maternal radiography much more frequently than singletons, the "directly causal" hypothesis must imply that the childhood cancer rate in twins in general will be larger than the rate in singletons in general (Burch, 1981; MacMahon, 1985). This argument is based on an unstated assumption that the childhood cancer rate in unirradiated twins and singletons is the same. There are well known biological differences between life *in utero* as a twin and as a singleton, in growth rate, mortality *in utero* and perinatally, maturity at birth, etc. There are also differences in childhood cancer rates. The overall rates of childhood cancer mortality in unirradiated singletons, DZ twins and MZ twins in the OCSS survey were 48, 37 and 11 per 100 000 (Table V). Differences of such magnitude must be taken into account. The overall rate of malignant disease, ignoring rates of exposure to radiography, was 5.06 per 10 000 singletons and 4.55 per 10 000 twins (DZ + MZ). There was a lower overall frequency in twins in spite of the 5–6 times greater frequency of radiography because cancer frequency in unirradiated twins was lower than in unirradiated singletons.

A further observation is that the proportional increase in cancer mortality rates in children exposed to radiography *in utero* as compared with other children is very similar for each different category of malignant disease. Such a constant proportional increase has not been found after irradiation at any post-natal age. This difference is said to cast doubt on the "directly causal" hypothesis, but this will be so only if there is some *a priori* reason for expecting that the relative sensitivity of different tissues to cancer induction by ionising radiation should be the same in the fetus as in the child or adult. Is there any independent evidence for this? About half the cancers that kill in childhood can be considered embryomas, specific types of cancer that are not seen at later ages; the other half are of types that also occur at later ages. Thus, there is no specifically

TABLE V

MALIGNANT DISEASE AFTER ANTE-NATAL RADIOGRAPHY. RATE PER 100 000 (MOLE, 1974)*

	Singleton births, 14.8 million (10% radiographed)	Dizygotic twins, 254 000 (55% radiographed)	Monozygotic twins, 99 000 (55% radiographed)
Not radiographed			
Leukaemia	22	16	Nil
Solid cancers	26	21	11
Total	48	37	11
Excess in the radiographed			
Leukaemia	12	9	29
Solid cancers	13	10	18

Correction of an arithmetical mistake in Mole (1974) has reduced the rates for leukaemia and solid cancers in non-radiographed singletons by 1 and increased the rate for solid cancers in radiographed singletons by 1.

*Liveborn 1945–64, England and Wales

high sensitivity of the individual *in utero* to induction by radiation of either class of malignancy.

Doll (1981), after reviewing the interpretative difficulties in studies of childhood cancer mortality in relation to radiographic exposure *in utero,* accepted the "directly causal" hypothesis. On the other hand, MacMahon (1985) did not, but his arguments against it have been reviewed here and found wanting. A continuing investigation of childhood cancer and antenatal radiography is in progress in the USA with the intention of comparing singleton births with the recently published case-control study of twins (Harvey et al, 1985; Harvey & Boice, 1985). Its results, whatever they turn out to be, should be illuminating

Sensitivity according to stage of gestation. The OCSS data suggest that the relative risk for radiography in the first trimester is several times larger than for the second and third trimesters (Bithell & Stewart, 1975; BEIR, 1980, p. 450) However, interpretation is not straightforward. Eighty per cent of the abdominal radiography in the first trimester was for non-obstetric reasons (Bithell & Stewart, 1975, their Table XIII) as compared with 5–8% for the whole of pregnancy. On average, non-obstetric abdominal radiography involved about five radiographs per examination, as against two for obstetric examinations, and some would have included fluoroscopy (cf. list of indications for radiography in Hewitt et al, 1966; Bithell & Stewart, 1975). When fluoroscopy was used the additional dose to embryo or fetus from this source is likely to have exceeded considerably the dose associated with the taking of, say, five radiographs. The specifically higher fetal tissue dose in non-obstetric radiography could account for much, if not for all, of the raised relative risk associated with exposure in the first trimester It would be helpful for radiological protection if subdivision of cancer induction by antenatal radiography at different stages of pregnancy was according to conceptus, embryo and early and late fetal stages, rather than according to trimester.

Concluding comment. When an individual *in utero* is exposed in the course of abdominal radiography of a mother, the whole body is likely to be irradiated. It is unusual for post-natal radiography at any age to irradiate more than a fraction of the whole body. There may, therefore, be good reason for special effort to limit radiography involving the fetus, even if overall tissue sensitivity to induction of malignant disease is similar in the fetus and in the adult.

ANIMAL EXPERIMENTATION AND ITS APPLICATION TO RADIOLOGICAL PROTECTION

The conceptus

The conceptus is the stage of development from the single-cell fertilised egg (zygote) to the stage when there is a placenta within the wall of the uterus. During the first week the human conceptus does not increase in size, even though cell division is occurring within its surrounding membrane. Towards the end of the first week it attaches itself to the inner surface of the uterus and begins to form the placenta in co-operation with maternal cells in the uterine wall (Williams & Warwick, 1980).

The single nucleus formed by fusion of the haploid nuclei from the sperm and oocyte divides into two, then into four and so on. Direct experiment in animals has shown that each cell of the two-cell stage and of the four-cell stage (sheep) has the complete potential for full development into a fully normal individual (Snow, 1986). Even at the eight-cell stage in the rabbit (Snow, 1986) and the 16-cell stage in the sheep a blastomere nucleus remains totipotent (Willasden, 1986). Thus, these early cell divisions produce a clone of cells according to the strict definition of the term "clone": a number of cells all derived from a single ancestor and with the same properties as each other. If the cells of a clone retain the ability to divide, then loss of some of the cells of a clone can be compensated for by additional divisions of surviving cells.

By the end of the fifth day the human conceptus consists of about 100 cells but fewer than one cell in 10, those forming the inner cell mass, will contribute directly to the future embryo and fetus. The other 90% will develop into the extraembryonic membranes, including the "embryonic part" of the placenta. Throughout its second week, the extraembryonic membranes form a similarly large proportion of the whole conceptus (Williams & Warwick, 1980). Experimental damage to cells fated to develop into extraembryonic membranes can be repaired by additional cell divisions of surviving cells.

These aspects of normal development have important radiobiological implications. The clonal character of the early conceptus implies that loss of one cell at the two-cell stage, of up to three cells at the four-cell stage etc. would not lead either to loss of the conceptus or to maldevelopment. How much further on in development this clonal character persists may not yet be known. The overall dimensions of the conceptus remain the same until the zona pellucida disintegrates at Day 7 p.c. Thus, the number of ionising tracks traversing it for a given dose will also remain the same, but an increase in number of cells with similar developmental potentialities will decrease the probability of developmental damage per unit dose. The conceptus enlarges during its second week of development, largely because of an accumulation of cell-free fluid, which is another factor tending to reduce the probability of radiation damage to an individual cell. During the first week the conceptus is about 100 μm in diameter and without a blood supply and so is likely to be hypoxic, given that oxygen diffuses no further than about 100 μm from a blood capillary in actively metabolising tissue. These various biological and radiobiological considerations are reasons why risk of loss of a conceptus from a given dose of ionising radiation may be lower than is sometimes feared and also why in experiments giving 100–200 cGy to the conceptus there is only "a slight

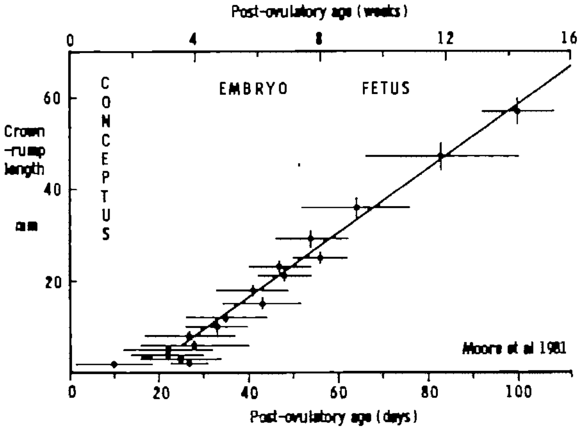

FIG. 3.

Crown–rump length of the human *in utero* during the first 100 days of gestation (data from Moore et al, 1981). The vertical and horizontal bar on each side of each point indicate the standard deviation of crown–rump length and post-ovulatory age, respectively. Each point, except the earliest and latest, is based on 20–52 specimens, the majority of which were of good quality Somites were first seen at 10 days. The mean number of somites reached 35 at 22 days, thereafter remaining at this (mean) value in each group until 100 days In 19% of all cases the embryos "appeared to be one cycle" out of phase "due to post-ovulatory bleeding or an absent last menstrual period " The adjusted, estimated post-ovulatory age, plotted above, was obtained by adjusting the apparent post-ovulatory age for these embryos by a single cycle. The 10 specimens where embryonic age was known exactly, because the date of a single coitus was known, gave a linear regression of crown–rump length on post-coital age (Fig. 1, Moore et al, 1981), virtually the same as shown in the diagram above

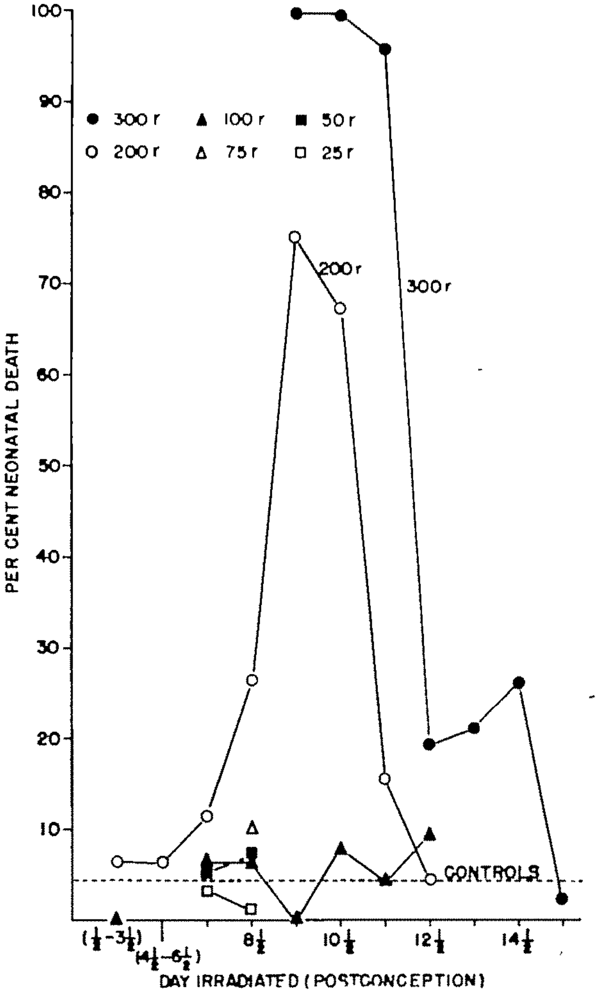

FIG 4

Percentage of neonatal mortality following X irradiation of mice *in utero* with different doses ("r" ≈ cGy) at different post-conceptional ages (Russell, 1954)

excess of abnormals in an irradiated group . . . It may be questioned whether 'they' are the result of direct radiation effects on the embryo" rather than mediated by maternal damage (Russell, 1965). There seems no reason to doubt the conclusion that irradiation of the pre-implantation stage of development "is virtually without risk of abnormality in a surviving child" (Russell, 1980).

The change from conceptus to embryo

Animal experiments show that, although the irradiated conceptus may die, malformation in a surviving conceptus is most unlikely and, in contrast, that malformations following experimental irradiation of the embryo are often seen. If these conclusions are generally applicable to mammalian development, it will be important to define the stage of development in the human species at which conceptus changes to embryo. The distinguishing feature of the embryo is the existence of a placenta but a period of time is required for the anatomical and functional development of the placenta after the beginning of implantation of the conceptus. This occurs in the human at about 8–9 days after fertilisation. Figure 3 illustrates the correlation between linear dimensions of the human conceptus, embryo and fetus and post-ovulatory age, based on several hundred presumptively normal specimens (Moore et al, 1981). Crown–rump length increases steadily from about 20 to 100 days post-conception, but comparatively very slowly before that. The fairly sudden increase in rate of "growth" at about 20 days p.c. suggests that it is not until then that the blood flow through the placenta has become well enough established to provide the nutritional support for embryonic growth. Thus, only from about 20 days on would the embryo be a well oxygenated and well fed population of cells capable of active cell division on a large scale and, therefore, of organogenesis. An inference might be that only from about 20 days on would the human embryo be fully sensitive to induction of malformations by ionising radiation.

This interpretation is an attempt to define a functional rather than a merely anatomical, or terminological, boundary between the stage of the conceptus and the embryo, a biological boundary which must be indistinct. To take just the bare experimental facts, that the embryo with a placenta is indeed sensitive to induction of malformations and that the conceptus before implantation is relatively much less sensitive, can lead to a somewhat arbitrary definition of the point in time when, for the purposes of radiological protection, the individual developing *in utero* is assumed to become radiosensitive to the induction of malformations. An example may be provided in L. B. Russell's recent discussion of radiological protection of the developing individual *in utero* in terms of a rule to limit medical diagnostic exposure. She wrote (Russell, 1980) "If I were to propose the rule today I should make it . . a 23-day rule", the 23 days being the sum of 14 days (the median time between onset of menstrual bleeding and the succeeding ovulation in normal women) plus 9 days where 9 days is (roughly) the pre-implantation period. Evidence that radiosensitivity to malformation induction in the human begins at the end of this 9-day period does not exist since there is no direct evidence about malformations produced by ionising radiation in the human species: inferences are, unavoidably, indirect.

The embryo and radiation-induced malformations

The literature is extensive (UNSCEAR, 1977b) and what follows is a highly selective consideration of a few important aspects.

The frequency of post-natal death after a single brief exposure of pregnant mice to 100 R X rays at each of seven different post-conceptional ages was virtually the same as in unirradiated controls (Russell, 1954; Russell & Russell, 1954). However, after 200 R at 8.5–11.5 days p.c. the frequency increased abruptly to 70–80%, and after 300 R virtually to 100% (Fig. 4). At these sensitive stages of gestation, the dose–response was highly non-linear. An example of a similar abrupt change in sensitivity with a small change in days p.c. at exposure is seen in the observations of Russell (1954) on morphological changes in the skeleton (Table VI). For example, the frequency of change in four different bones of the appendicular skeleton, forearm long bones, clavicle, ileum and femur, after 300 R given on Day 9.5 p.c. was zero, given on Day 10.5 was 50–90% and given on Day 11.5 was, again, zero. But what seems never to have been emphasised is the corresponding and dramatic non-linearity of response. After 200 R at day 10.5, a sensitive stage, the frequency was zero in three of the bones and 5% in the fourth, as against 50–90% after 300 R. The other six of the 10 bones tabulated show the same extreme non-linearity of response on the day of maximum sensitivity to 300 R, whatever that day happened to be (Table VI).

If these experimental results are to be used for the purposes of radiological protection, the extremely non-linear dose–responses are surely much more significant than the existence of "critical stages of development" with high sensitivity to induction of malformations. These "critical" stages of enhanced sensitivity were not seen at 200 R in the bones listed in Table VI and, therefore, would not be expected at any lower level of exposure. It should be stressed that the highly non-

TABLE VI

FREQUENCY (%) OF MALFORMATIONS OF SELECTED BONES IN NEWBORN F1 MICE AFTER A BRIEF EXPOSURE TO X-RAYS *IN UTERO* AT DIFFERENT POST-CONCEPTIONAL AGES (ADAPTED FROM RUSSELL, 1954)

	Post-conceptional day of brief exposure to X rays							
	9.5		10.5		11.5		12.5	
Exposure (R)	200	300	200	300	200	300	200	300
Forelimb long bones	0	0	0	90	0	0	0	0
Clavicle	0	0	0	50	0	0	0	0
Scapula	0	60	0	70	0	0	0	0
Sternum	8	100	3	80	0	0	0	0
Pelvis								
Ilium	0	0	5	60	0	0	0	0
Ischium	0	0	0	0	0	40	0	0
Pubis	0	0	0	0	0	30	0	0
Hind limb								
Femur	0	0	0	85	0	0	0	0
Tibia	0	5	0	70	0	0	0	0
Fibula	0	0	3	100	0	25	0	0

Russell (1954) presented her findings in diagrams. The percentage values in this table have been read off the diagrams and so cannot be exact.

linear dose–responses under discussion cannot be understood in terms of simple cellular considerations.

Scoring morphological abnormalities

A variety of abnormalities will be seen in any individual experiment and will be classified according to the investigator's criteria. It is a common practice (many examples are to be found in UNSCEAR, 1977b) to add up the frequencies of each separate category of abnormality and to use the "percentage of abnormalities" so obtained as the overall measure of the degree of radiation damage. Quite often, these total percentages are plotted as if 100% was the maximum rate. If this system of scoring is applied to the data on morphological changes in bones in Table VI the "score" for 300 R received at 10.5 days p.c. as obtained by simple addition is 605% for the 10 bones tabulated, and would be still larger if all the other bones examined in the same animals (Russell, 1954) were included. The "score" would be further increased if the category "forelimb long bones" (Table VI) was subdivided according to its component parts In fact, the system of simple addition of percentages is quite arbitrary and meaningless.

For the purposes of radiological protection, the solution to the problem seems clear. It is to consider results in terms of the proportion of individuals free from any of the abnormalities the investigator is detecting and recording Alternatively, and really the same thing, to present results in terms of the proportion of individuals with one or more malformations (as in Fig. 6 of Di Majo et al, 1981) However, very few investigators have provided their results in either of these forms and it is impossible to make deductions from the usual tabulation of data, since there is no way of telling how many of the recorded malformations were found in one and the same individual.

The clonal hypothesis for organogenesis and its impact on risk assessment

When Snow (1981b) administered

> "mitomycin C (which causes more-or-less random cell death by interference with DNA synthesis) at 6.5–7.5 days p.c., *i.e.* post-implantation and at the earliest stages of organogenesis, the total number of cells in a mouse embryo was reduced to 10–15% of normal. Nevertheless, a substantial fraction of such treated embryos developed into normal adults (30–40%, Snow, 1986), suggesting a minimum clone size for an organ primordium of some 10 cells. Detailed studies of treated embryos showed no immediate disturbance of morphogenesis but then a transient mis-match between the development of different regions of the embryo coupled with a marked increase in mitotic rate in all tissues to well above normal values. Within a week this 'catch-up' growth resulted in an embryo of normal morphology and normal size, except for the gonads This exception accounted for the only abnormality found in the apparently normal adults: they were commonly, but not always, sub-fertile or infertile (Snow, 1981b)" (Mole, 1984).

Twenty years previously, almost the same language had been used by Hicks and D'Amato (1961) in relation to catch-up growth in the irradiated CNS:

> "... virtually normal regeneration of the neural folds results after irradiation around ten somites, and of the retina after irradiation at 40 somites, even though the majority of the cells of these structures had been wiped out by the radiation." "...'catch-up' growth and restoration of morphological normality after substantial random cell death in the embryo" could well "explain the steep dose–response for frequency of abnormalities after embryonic irradiation. A striking parallel between mitomycin C and ionizing radiation is that irradiation of mouse embryos with doses which cause little prenatal mortality and allow normal development to adult ages may nevertheless make these adults sub-fertile or completely sterile (UNSCEAR, 1977b; Snow, 1981b)" (Mole, 1984).

Indeed, it is difficult to imagine any explanation applicable both to Snow's findings with mitomycin C and the experimental observations on radiation damage other than a clonal hypothesis for organ development in the embryo

Such a hypothesis fits well the observations of Russell (1954) on morphological abnormalities in the bones of irradiated embryos. With $\lambda = 0.001\ \mathrm{mGy}^{-1}$ the survival fraction of cells according to the equation $\exp(-\lambda D)$ after 200 or 300 R (taken to equal 2 and 3 Gy) would be 0.14 and 0.05, respectively. Thus, in a clone of 10 cells, 1.4 cells, on average, would survive after 200 R and 0.5 cells, on average, after 300 R. The possibility of replenishing the clone by accelerated division of surviving cells would be high after 200 R and poor after 300 R. A Poisson mean of 1.4 cells implies that no surviving cells would be found in 18% of a number of independent clones, and a mean of 0.5 that 61% would contain no survivors. These values are reasonably near the observed values for percentages of animals with abnormalities of bones: 0–8% after 200 R and 50–100% after 300 R (Table VI).

The clonal hypothesis implies that the developmental fate of a cell is common to a number of equipotential cells (the clone) which are stem cells in the sense that each has the ability to replace itself or any other member of the clone and can do this by additional unscheduled cell divisions over and above the cell divisions required in the course of normal, undisturbed development. As normal embryonic development proceeds, individual cells become more specialised, losing the wider potentialities for development possessed by their ancestor cells The clonal hypothesis states that loss of wider potentialities occurs several cell divisions later than might be supposed otherwise. It implies that loss of cells will not impair development unless it exceeds a threshold level and that a newly sensitive stage of embryonic development will be found whenever, in the course of normal development, the number of cells in a clone (with a given developmental fate) and/or their ability to replace themselves by additional unscheduled cell divisions has been sufficiently reduced. As the cells in a clone continue to multiply in the course of normal development, sensitivity to maldevelopment caused by induced or spontaneous loss of cells will decrease. If $\lambda = 0.001\ \mathrm{mGy}^{-1}$, a single stage of cell division increasing cell number in a clone, from, say, five to 10 or 10 to 20, would increase by 69 R the radiation exposure required to produce, say, 50% abnormality, and two successive cell divisions by 139 R. Given that a cell can divide once or twice in a day, the clonal hypothesis makes it easy to understand that change by 24 h in the day p.c. of an exposure could cause a marked change in the frequency of induced abnormality (Fig. 4 and Table VI). A clonal hypothesis may provide an acceptable means of extrapolation from experimental results for purposes of radiological protection.

The calculations presented are extremely simplified: it is not known whether more than a single cell has to survive before a clone can be replenished fast enough and whether clone size and the rate of unscheduled cell divisions are different in different embryonic clones with different developmental fates. Russell (1954) and Russell and Russell (1954) set out the principle of calculating clone size in the context of explaining apparently variable results in frequency of abnormalities "even in perfectly uniform material". However, they did not refer to the possibility that the same concept would indicate that induction of abnormalities might have a real threshold when the level of radiation exposure is low enough.

Nearly all the experimental observations relating to a substantial frequency of abnormalities after embryonic irradiation are after doses in the range 1–3 Gy (UNSCEAR, 1977b). In the minority of investigations where smaller doses were used, the dose–response has been curvilinear, not linear. If a clonal concept is accepted as a general hypothesis for organogenesis in development, then linear extrapolation downwards from doses in the range 1–3 Gy must be invalid. Furthermore, whether a clone numbers five, 10 or 20 cells, the effect of 10 mGy is bound to be of little consequence, even if the intrinsic radiosensitivity of cells (*i.e.* λ in $e^{-\lambda D}$) is an order of magnitude greater than that assumed for the calculations above.

A clonal hypothesis also makes it easier to understand other observations. Protraction of a given radiation exposure commonly reduces the frequency of induced abnormalities (UNSCEAR, 1977b). As protraction of an exposure increases, there would be more and more time for replacement of lost cells by additional unscheduled divisions of surviving cells. The human conceptus and embryo grow relatively slowly: 8 weeks are needed to reach a mass of about 1 g as compared with 2 weeks in mouse, rat, hamster and rabbit (Snow, 1981a). A slower development rate will allow more opportunity for catch-up growth, if this is needed, a possible reason why abnormalities after irradiation of the human embryo seem so uncommon as compared with their high frequency after embryonic irradiation of experimental animals by sufficiently large doses. In the work of Russell (1954), frequency of abnormalities in small bones, such as ribs and vertebrae, after embryonic irradiation of mice on the most sensitive day p.c., reached 50–100% after 200 R, whereas 300 R was required in larger bones (Table VI). Could this difference arise because the clones of origin of the small bones contain fewer cells than the clones of larger bones?

Snow (1983) regarded the mismatch of normal morphology during the catch-up growth phase following damage to the embryo as the likely basis for teratogenesis and thought a clonal hypothesis unlikely. If each cell type surviving irradiation, mitomycin C, or other damaging agent, increases its cell division rate autonomously and not in a co-ordinated fashion, then mistiming of inductive interactions between tissues can be expected. To me, that does not exclude a clonal hypothesis; indeed, it is one way in which a clonal hypothesis could express itself, via an abnormally increased clone size as an alternative mechanism to a mere deficiency in number of constituent cells. The inferences to be drawn for the purposes of radiation protection may not seem to be affected, except in one important direction. The inference from the clonal hypothesis, that there will be a threshold for induction of abnormalities, cannot be substantiated for Snow's hypothesis in the absence of quantitative understanding of the influence of mistiming of inductive interactions between tissues.

High-LET radiation

If frequency of abnormality depends on two factors, a reduction in number of cells in a clone to some threshold value and a repopulation of the clone by division of surviving cells, then the reduction of cell numbers per unit dose will depend on LET but the efficiency of repopulation by division of surviving cells will be independent of LET since the cells involved are survivors. The number of ineffective clones (with fewer cells than the minimum needed for restoration to normal) and their distribution between different individuals will determine curvilinearity over the response range up to, say, 60% or higher, whatever the LET may be and without the need to invoke a shoulder on the cell survival curve. This expectation is well illustrated in the work of Cairnie et al (1974), who found the same highly curvilinear response (with apparent threshold) both with $^{60}\mathrm{Co}$ γ rays and with fission neutrons for most specific abnormalities seen in mice after exposure at 11 days p.c. (*loc. cit.* Fig. 3 and

Table 5) The most extensive comparisons of exposure *in utero* to fission neutrons and low-LET radiation over a wide range of dose down to 5–6 rad is by Di Majo et al (1981). For irradiation of mice at 7.5 days p c., the response was curvilinear for neutrons as well as for X rays when damage was expressed as frequency of fetuses with one or more abnormalities (*loc. cit.* Fig. 6) However, there was a definite, if relatively small, effect at relatively small doses for both qualities of radiation which would have been predicted on a clonal hypothesis only if the relevant clones contained only a very few cells. After 5–80 rad of X rays or 6–18 rad of fission neutrons the pooled incidence of the first subgroup of malformations was 0.9% and 0.7% as against zero in unirradiated controls (omitting the animals with phocomelia, all of which were seen in a single experimental run). The pooled incidence of the second subgroup of malformations was 4.7% and 4.7% as against 1.5% in the controls.

These experimental observations on embryonic damage by high-LET radiation may become relevant to radiological protection if the current revision of the Japanese atomic-bomb dosimetry, when completed, fails to reconcile the apparent difference between Hiroshima and Nagasaki in the dose-dependence of severe mental retardation in those exposed *in utero*.

Final Comments

This review has identified several aspects of development *in utero* where the quantification of radiation damage seems to depend on the interaction of ionising radiation with a clone of cells rather than with a single cell, as in the conceptus and embryo. This possibly novel concept may be applicable to other forms of detriment based on polycytic (non-stochastic) damage following post-natal irradiation. A clonal mechanism predicts a virtual threshold of dose below which radiation damage is completely reparable.

If the frequency of induced malignant disease in Japanese bomb survivors exposed post-natally continues to increase with continuing follow-up, the post-natal sensitivity to cancer induction will come to exceed the pre-natal sensitivity, according to conventionally linear risk estimates per unit tissue dose. However, if linearity is not the correct basis for extrapolation from large to smaller doses when considering carcinogenesis, current conclusions about relative sensitivity to carcinogenesis *in utero* and post-natally can only be provisional.

There is, at present, no convincing evidence that the embryo and early fetus are more sensitive to induction of malignant disease than later stages of pregnancy and, thus, no reason on the grounds of supersensitivity of the fetus to reintroduce a specific limitation on medical radiography or occupational exposure of pregnant women based on carcinogenesis instead of teratogenesis. Nevertheless, abdominal radiography in pregnancy is more carcinogenic, dose for dose, than virtually all other radiography because all the tissues of the individual *in utero* are irradiated instead of merely a fraction of the body volume.

Given the limited amount of pertinent information currently available, it seems premature to attempt an assessment of sensitivity of the first 8 weeks of the fetal stage of development to impairment of post-natal mental function. A great deal of new information with the potential for direct application to radiological protection should become available in the near future.

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Principles of the International Commission on Radiological Protection system of dose limitation

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ABSTRACT

The current recommendations of the International Commission on Radiological Protection (ICRP), published in 1977, identify two types of effect against which protection is required. "Stochastic" effects are those for which the probability of an effect occurring, rather than its severity, is regarded as a function of dose without threshold, whereas "non-stochastic" effects are those for which the severity varies with the dose and for which a threshold may occur The system of dose limitation recommended by the ICRP is based on the prevention of non-stochastic effects and limitation of the probability of stochastic effects to levels deemed to be acceptable. The prevention of non-stochastic effects is achieved by setting dose-equivalent limits at values such that no threshold dose would be reached, even following exposure for the whole of a lifetime or for the total period of a working life. The limitation of stochastic effects is achieved by keeping all justifiable exposures as low as is reasonably achievable, economic and social factors being taken into account, subject to the constraint that reductions in collective exposure do not cause unacceptably large individual exposures.

The formulation of a quantitative system of dose limitation based on these principles requires that judgments be made on several factors including: relationships between radiation dose and the induction of deleterious effects for a variety of end-points and radiation types; acceptable levels of risk for radiation workers and members of the public; and methods of assessing whether the cost of introducing protective measures is justified by the reduction in radiation detriment which they will provide In the case of patients deliberately exposed to ionising radiations, the objectives of radiation protection differ somewhat from those applying to radiation workers and members of the public. For patients, risks and benefits relate to the same person and upper limits on acceptable risks may differ grossly from those appropriate to normal individuals For these reasons, and because of its historical relationship with the International Congress of Radiology, the ICRP has given special consideration to radiation protection in medicine and has published reports on protection of the patient in diagnostic radiology and in radiation therapy

It is generally accepted that exposures to ionising radiations can lead to a wide spectrum of deleterious effects in man. Thus, in 1951, the International Commission on Radiological Protection (ICRP) stated (ICRP, 1951):

"It appears that the effects to be considered are:

(1) Superficial injuries.

(2) General effects on the body, particularly the blood and blood-forming organs, *e.g.* production of anaemia and leukemias.

(3) The induction of malignant tumours.

(4) Other deleterious effects including cataract, obesity, impaired fertility, and reduction in lifespan.

(5) Genetic effects."

With the exception of obesity and, possibly, non-specific reduction in lifespan, this list continues to represent a reasonable judgment as to the types of effects induced by ionising radiations.

In its most recent basic recommendations (ICRP, 1977a), the ICRP identified two general classes of effect against which protection is required. These two classes are termed "stochastic" and "non-stochastic". Stochastic effects are those for which the probability of the effect occurring, rather than its severity, is regarded as a function of dose without threshold, whereas non-stochastic effects are those for which the severity of the effect varies with the dose and for which a threshold may, therefore, occur. Stochastic effects are taken to include cancer and the induction of hereditary effects in the descendents of the irradiated individual. The system of dose limitation recommended by the ICRP is based on the prevention of non-stochastic effects and the limitation of the probability of stochastic effects to levels deemed to be acceptable.

It should be noted that effects of constant severity which have a threshold of induction are included neither as stochastic nor as non-stochastic effects. In practice, this is not a substantial limitation, since it cannot be demonstrated that any such threshold exists for the induction of cancer or of hereditary effects.

In order to prevent non-stochastic effects and limit the probability of stochastic effects to levels deemed to be acceptable, the Commission recommends a system of dose limitation with the following main features.

(a) No practice shall be adopted unless its introduction produces a positive net benefit.

(b) All exposures shall be kept as low as reasonably achievable, economic and social factors being taken into account.

(c) The dose equivalent to individuals shall not exceed the limits recommended for the appropriate circumstances by the Commission.

In this paper, the various stochastic and non-stochastic effects considered by the Commission in its

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* The opinions expressed in this paper are those of the author, and not necessarily those of the ICRP

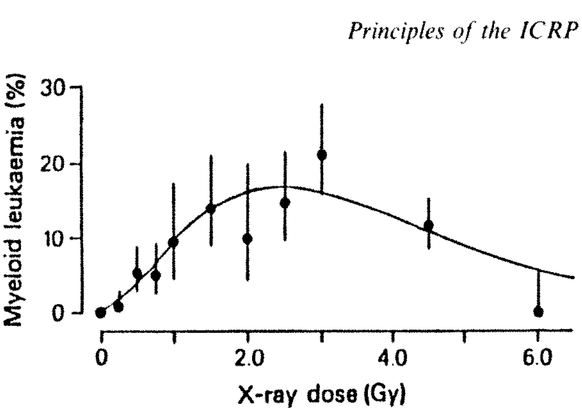

FIG. 1

Myeloid leukaemia frequency (±80% binomial confidence limits) after whole-body exposure of male CBA/H mice to 250 kVp X rays. The fitted curve is $24 D^2 \exp(-0.825 D)$, with indicence in per cent and dose in gray. From Mole et al (1983).

basic recommendations are discussed and the simplifying assumptions adopted for radiological protection purposes are identified. The complete dose limitation system developed for radiation workers and members of the public is summarised and modifications to this system relevant to the irradiation of patients are discussed. Some topics which will require consideration in any future revision of the Commission's recommendations are identified.

THE LIMITATION OF STOCHASTIC EFFECTS

It is a general observation in radiobiology that dose–response relationships are curvilinear and may exhibit both ascending and descending portions. An excellent illustration of this is the induction of myeloid leukaemia in CBA mice by single acute doses of X rays (Mole et al, 1983). As shown in Fig. 1, the dose–response relationship in this case initially curves upward, reaches a peak and then declines. This pattern is attributed to an interaction between a monotonically increasing induction term and the effects of cell sterilisation at high doses, since cells incapable of division cannot give rise to cancers.

The ICRP (1977a) has taken the view that the effects of cell sterilisation are not significant at the doses encountered in normal exposure conditions, except in so far as they may reduce the risks of irradiation by highly-localised incorporated radionuclides, *e.g.* insoluble particulate material in the lungs. Furthermore, the Commission states that "there are radiobiological grounds for assuming that the dose–response curve for low linear energy transfer (LET) radiation will generally increase in slope with increasing dose and dose-rate over the absorbed dose range up to a few gray" and that "for many effects studied experimentally, the response in this range can be represented by an expression of the form:

$$E = aD + bD^2 \qquad (1)$$

where E denotes the effect, D the dose and a and b are constants".

For the purposes of radiation protection, the Commission assumes that Equation 1 can be simplified to:

$$E = aD \qquad (2)$$

i.e. that there is a linear relationship between dose and effect without threshold. Justification for this simplification is that the doses of interest in radiation protection are generally relatively small and/or are delivered at low dose-rates.

This assumption of linearity and absence of dose-rate effects permits considerable simplifications in radiation protection. Thus, the effect of two increments of dose, ΔD_1 and ΔD_2, is given by:

$$E = a(\Delta D_1 + \Delta D_2) = a\Delta D_1 + a\Delta D_2 = \Delta E_1 + \Delta E_2 \qquad (3)$$

i.e. individual increments of dose can be considered separately. This means that the collective detriment from any source of exposure due to stochastic effects can be considered separately from the collective detriment from any other source, including natural background. It also means that the radiation exposure of an individual from a practice can be controlled by consideration of his current levels of exposure, without a detailed knowledge of past levels.

Accepting the practice of using a linear dose–response relationship without threshold, it is then necessary to derive values of the slope of that relationship for various end-points and radiation types. In regard to this, the ICRP (1977a) commented that "for human populations . . . knowledge of dose–response relationships is too limited to enable confident prediction of the shapes and slopes of the [dose–response] curves at low doses and dose rates". Thus, in many instances, risk estimates depend on data derived from irradiation involving higher doses delivered at high dose-rates. Nevertheless, the ICRP has made an effort to take this factor into account and has stated (ICRP, 1978) that its risk factors "are intended to be realistic estimates of the effects of irradiation at low annual dose equivalents (up to the Commission's recommended dose-equivalent limits)".

It should be noted that the risk factors used generally apply to the mean dose equivalent over the entire organ or tissue under consideration, as well as being the values obtained by averaging over both sexes and over a range of ages at exposure (ICRP, 1977a). This averaging, over age and sex, though of considerable importance for some particular risks, *e.g.* for the induction of breast cancer, is of only limited significance for most exposure regimes, since a number of organs and tissues are generally irradiated to a greater or lesser extent. The risk factors estimated by the ICRP (1977a, 1978) on the above basis are summarised in Table I. Some comments on these risks are appropriate.

(a) The risk of hereditary effects applies only to the first two generations of offspring. If risks to all

TABLE I

RISK FACTORS

Organ or tissue	Risk (Sv^{-1})	Comments
Gonads	4×10^{-3}	Serious hereditary effects in the first two generations of offspring
Red bone marrow	2×10^{-3}	Fatal leukaemia
Endosteal cells on bone surfaces	5×10^{-4}	Fatal osteosarcoma
Lung	2×10^{-3}	Fatal lung cancer
Thyroid	5×10^{-4}	Fatal thyroid cancer
Breast	2.5×10^{-3}	Fatal breast cancer
Skin	1×10^{-4}	Fatal skin cancer
Other tissues	$<5 \times 10^{-3}$	Fatal cancer

generations were included, the value would be approximately double that shown.

(b) Only risks of fatal cancer are included, with no account being taken of the risk of inducing curable cancers. As discussed in ICRP Publication 45 (ICRP, 1985c), this subject has been reviewed by UNSCEAR, using, whenever possible, as a criterion of cure, the percentage of patients with different types of cancer who were surviving at 15 years after diagnosis, and following surgical or other treatment (in countries with developed medical facilities). The estimates obtained are shown in Table II. Except for thyroid and skin, inclusion of non-fatal cancers would not increase the risk estimates substantially.

(c) For bone, the radiosensitive cells have been identified as the endosteal cells and epithelial cells on bone surfaces (ICRP, 1968). In order to undertake dose calculations for internally incorporated radionuclides, many of which deposit preferentially in skeletal tissues, it is necessary to give a more precise geometrical description of the tissue at risk. The definition selected is of a 10 μm thick layer covering all endosteal surfaces and surfaces lined with epithelium (ICRP, 1979a). The adequacy of this definition needs further consideration, since only a limited amount of work has been undertaken on the localisation of the cells at risk. However, the induction of osteosarcomas in workers exposed to ^{226}Ra (*e.g.* Evans, 1974) and in patients exposed to ^{224}Ra (*e.g.* Spiess & Mays, 1973) indicates that a substantial fraction of the cells at risk must lie within about 40 μm of the bone surface (see also Thorne, 1977).

(d) Amongst other tissues, the ICRP (1977a) identified some (*e.g.* stomach, lower large intestine, salivary glands and probably liver) for which there was evidence that radiation is carcinogenic at moderate doses. However, the Commission did not attempt to assign risk factors to individual tissues, but did estimate that no single tissue is responsible for more than one fifth of the total.

(e) The risk factors are expressed in terms of dose equivalent rather than absorbed dose. These two quantities are related using the expression:

$$H = DQN \qquad (4)$$

where H is the dose equivalent at a particular point, D is the absorbed dose at that point, Q is the quality factor of the radiation and N is the product of all other modifying factors (currently always taken as unity). It should be noted that Q is dependent only upon the type of radiation. Thus, the Commission implicitly assumes that the relative biological effectiveness of two different types of radiation, over the dose range of interest in radiation protection, can be represented by a single value, irrespective of the end-point under consideration.

These risk factors are not used directly by the Commission in its recommendations. Instead, they are summed to give a total risk factor of 0.0165 Sv^{-1} for uniform whole-body irradiation. Non-uniform irradiation is then treated by the calculation of an effective dose equivalent, H_E (ICRP, 1978), defined by:

$$H_E = \sum W_T H_T \qquad (5)$$

where H_T is the dose equivalent in organ or tissue T and W_T is the weighting factor for that organ or tissue.

Values of W_T are calculated as the ratio of the individual organ or tissue risk factor to the total risk factor for uniform whole-body irradiation and the values recommended by the Commission are listed in Table III. Two comments are required on this list.

(a) Because the Commission estimated that no single tissue is responsible for more than one fifth of the total risk arising from other tissues when the body is

TABLE II

ESTIMATES OF PATIENTS SURVIVING 15 YEARS

Cancer	15-year survival (%)
Breast	40
Leukaemia	$\simeq 5$
Lung and bronchus	<5
Thyroid	91–97
Bone	20
Skin	>95 (possibly >99)
All other tissues	$\simeq 25$

TABLE III

WEIGHTING FACTORS

Organ or tissue	W_T
Gonads	0.25
Breast	0.15
Red bone marrow	0.12
Lung	0.12
Thyroid	0.03
Bone surfaces	0.03
Remainder	0.30

TABLE IV

POTENTIAL ANNUAL DOSES TO INDIVIDUAL ORGANS

Organ or tissue	W_T	Maximum annual dose (Sv) based on limitation of stochastic effects only
Gonads	0.25	0.20
Breast	0.15	0.33
Red bone marrow	0.12	0.42
Lung	0.12	0.42
Thyroid	0.03	1.67
Bone surfaces	0.03	1.67
Any one organ or tissue in remainder	0.06	0.83

irradiated uniformly, it recommended that a value of W_T of 0.06 is applicable to each of the five organs or tissues of the remainder receiving the highest dose equivalents and that the exposure of all other remaining tissues can be neglected. If the Commission's assumption is correct, this rule will invariably overestimate the significance of tissues of the remainder.

(b) Skin is excluded, since it was not included in the table given in the basic recommendations of the Commission (ICRP, 1977a). However, in a subsequent statement (ICRP, 1978), it was noted that in the assessment of detriment from exposure of population groups a small risk of fatal cancer from exposure of the skin may need to be taken into account, and a weighting factor of about 0.01 was suggested.

Using the formalism set out above, limitation of the risk of inducing stochastic effects can be achieved by controls on effective dose equivalent. In order to prevent undue exposure of individuals, limiting values of effective dose equivalent can be defined and practices can be optimised by considering trade-offs between collective effective dose equivalent and other factors, such as the cost of protection (see below).

For radiation workers, the Commission considered (ICRP, 1977a) that for the foreseeable future a valid method for judging the acceptability of the level of risk in radiation work is by comparing this risk with that for other occupations recognised as having high standards of safety. At that time, this was considered to be those occupations for which the average annual mortality did not exceed 10^{-4}. In order to compare radiation risks with this figure, the ICRP stated that:

> "In the case of uniform exposure of the whole body, in circumstances where the Commission's recommendations, including the annual dose-equivalent limit of 50 mSv, have been applied, the distribution of the annual dose equivalents in large occupational groups has been shown very commonly to fit a log-normal function, with an arithmetic mean of about 5 mSv, and with very few values approaching the limit. The application of the risk factors . . . to the above mean dose indicates that the average risk in these radiation occupations is comparable with the average risk in other safe industries."

In fact, an annual dose of 5 mSv, together with a risk factor of 0.0165 Sv^{-1}, corresponds to an annual risk of 8×10^{-5}. Thus, having made this comparison, the Commission felt justified in making no change to the recommended dose limit for workers.

For members of the public, acceptable risks were inferred from consideration of risks which an individual can modify to only a small degree, but which may be regulated by national ordinance. On this basis, a risk of 10^{-6} to 10^{-5} per year was regarded as likely to be acceptable to any individual member of the public (ICRP, 1977a) In its basic recommendations (ICRP, 1977a), the Commission concluded that such a level of acceptable risk implied the restriction of the lifetime dose to an individual to a value that would correspond to 1 mSv per year of life-long whole-body exposure, but considered that the Commission's previously recommended dose-equivalent limit of 5 mSv in a year, as applied to critical groups, would provide this degree of safety. Recently, the Commission has modified its advice on this topic and, in the statement from its 1985 Paris meeting (ICRP, 1985a), has stated that:

> "The Commission's present view is that the principal limit is 1 mSv in a year. However, it is permissible to use a subsidiary dose limit of 5 mSv in a year for some years, provided that the average effective dose equivalent over a lifetime does not exceed the principal limit of 1 mSv in a year."

Thus, under this recommendation, even the most exposed individual would not receive more than 1 mSv per year on a long-term basis, corresponding to an annual risk of 1.65×10^{-5}, and most individuals would be exposed at lower, or considerably lower, levels. For this reason, annual risks to members of the public will, necessarily, not exceed the range of values judged acceptable by the ICRP.

THE LIMITATION OF NON-STOCHASTIC EFFECTS

The limitation of stochastic effects, discussed in the previous section, implies that, in principle, individual organs and tissues of radiation workers could receive annual doses of $0.05/W_T$ Sv, if only a single organ or tissue were irradiated. In practice, such grossly inhomogeneous irradiation seldom occurs, though some cases, such as the inhalation or ingestion of ^{131}I, which result predominantly in thyroid exposure (ICRP, 1979b), can be envisaged.

Annual doses which could be received by individual organs and tissues, if limitation of stochastic effects were the only consideration, are listed in Table IV.

In order to prevent non-stochastic effects, the Commission (ICRP, 1977a) recommended a dose-equivalent limit of 0.5 Sv in a year to all tissues except the lens, for which the Commission recommended a limit of 0.3 Sv. Subsequently (ICRP, 1980a), because of consideration of the possibility of induction of lens opacities which though themselves not detrimental to vision might develop further without additional exposure, the Commission decided to recommend a reduction in the dose limit to the lens to 0.15 Sv in a year.

Other than for the skin and lens of the eye, the basic recommendations of the Commission (ICRP, 1977a) gave little justification for the value of the non-stochastic limit which had been selected. This weakness in the Commission's recommendations became particularly noticeable with the appearance of ICRP Publication 30 (ICRP, 1979a; 1980b; 1981), since it was found that annual limits on intake (ALIs) for a substantial number of important radionuclides were determined, albeit sometimes only marginally, by the non-stochastic limit.

However, the Commission has now published a detailed review of the non-stochastic effects of ionising radiations (ICRP, 1984b) and has concluded that:

> "Presently recommended dose-equivalent limits provide a substantial margin of safety for all tissues with the possible exception of the bone marrow, gonads and lens of the eye... In the case of the testis and bone marrow, protraction of exposure over decades should minimise the effect of occupational irradiation, because spermatogenic and hematopoietic cells are highly capable of regeneration and repopulation. For the ovary and lens, however, annual exposure at the dose limits might conceivably lead to cumulative doses approaching the thresholds for non-stochastic effects, although it is highly improbable that these tissues would receive the dose limit annually year after year in any radiation worker".

It should be noted that the system of dose limitation for both stochastic and non-stochastic effects uses the quantity dose equivalent. Thus, it is implicitly assumed that the influence of LET is the same for both types of effect. The ICRP (1984b) has considered this point and has concluded that there is no evidence that present values of Q need to be revised upward for non-stochastic effects, but has emphasised that the relevant data are fragmentary.

In regard to members of the public, the Commission has stated (ICRP, 1985a) that, with the limitation on average annual effective dose equivalent to 1 mSv per year, a non-stochastic dose limit is unnecessary for most organs. However, since dose equivalents to skin and lens of the eye are not included in the computation of effective dose equivalent, organ dose limits are still needed for these two tissues and a value of 50 mSv has been selected. This limit is considerably lower than the values of 0.5 Sv and 0.15 Sv, for skin and lens respectively, which are used for radiation workers This reduction was justified (ICRP, 1977a) by consideration of the longer exposure period and practical difficulties in controlling the total exposure from all sources for a member of the public An additional factor which may need to be taken into account, but which is not mentioned by the ICRP, is possible variations in sensitivity with age and health status. Such variations are likely to be larger in the general public than in a work force.

Optimisation

In limiting the incidence of stochastic effects from radiation exposures, it is not, in general, sufficient only to achieve compliance with the dose limits. An integral part of the Commission's recommendations is that all exposures shall be kept as low as is reasonably achievable, economic and social factors being taken into account. In its basic recommendations (ICRP, 1977a), optimisation was taken to be virtually synonymous with cost-benefit analysis, but this is not the case and many other techniques do exist (see, for example, Oudiz et al, 1981).

Nevertheless, cost-benefit analysis is currently the major tool used in optimisation of protection and has, therefore, been given considerable attention by the Commission (ICRP, 1983). The basic principle (ICRP, 1977a) is that the net benefit, B, of a product or an operation involving irradiation can be regarded as equal to the difference between its gross benefit, V, and the sum of three components: the basic production cost, P, the cost of achieving a selected level of protection, X, and the cost, Y, of the detriment involved in the operation, or in the production, use and disposal of the product, so that:

$$B = V-(P+X+Y) \tag{6}$$

Assuming that V and P are independent of the level of protection, the net benefit, which must be positive for justification of the practice, is optimised at that value (S^*) of collective effective dose equivalent, S, for which:

$$\left.\frac{\mathrm{d}X}{\mathrm{d}S}\right|_{S^*} = -\left.\frac{\mathrm{d}Y}{\mathrm{d}S}\right|_{S^*} \tag{7}$$

Often, the collective effective dose equivalent will be determined by a single protection parameter, w, such as the thickness of a shielding wall. In such a case:

$$\frac{\mathrm{d}X}{\mathrm{d}S} = \frac{\mathrm{d}X}{\mathrm{d}w}\bigg/\frac{\mathrm{d}S}{\mathrm{d}w} \tag{8}$$

and similarly for $\mathrm{d}Y/\mathrm{d}S$.

Thus, substituting into Equation 7, optimisation is achieved at a value of the protection parameter, w^*, such that:

$$\left.\frac{\mathrm{d}X}{\mathrm{d}w}\right|_{w^*} = -\left.\frac{\mathrm{d}Y}{\mathrm{d}w}\right|_{w^*} \tag{9}$$

In this equation, X and Y must be expressed in the same units. Thus, since X is a monetary cost, Y must also be expressed in monetary terms.

Now, Y is the detriment due to the radiation exposure and may reasonably be related to the distribution of individual doses received as a result of the practice under consideration. Thus,

$$Y = \int_0^{H_E^{\mathrm{Max}}} \mathrm{N}(H_E)\,\mathrm{F}(H_E)\,\mathrm{d}H_E \qquad (10)$$

where H_E^{Max} is the maximum effective dose equivalent received by any individual in the irradiated population, $\mathrm{N}(H_E)\,\mathrm{d}H_E$ is the number of individuals associated with effective dose equivalents of between H_E and $H_E+\mathrm{d}H_E$ and $\mathrm{F}(H_E)$ is a weight function which represents the monetary value of the detriment associated with an effective dose equivalent of H_E.

If the detriment is taken to be directly proportional to the dose received, corresponding to a direct proportionality with incurred risk on the no-threshold linear dose–response relationship hypothesis for stochastic effects, it is possible to write:

$$\mathrm{F}(H_E) = \alpha H_E \qquad (11)$$

where α has dimensions of monetary cost per unit dose and is typically expressed in units such as £ Sv^{-1}.

Substituting Equation 11 into Equation 10:

$$Y = \int_0^{H_E^{\mathrm{Max}}} \alpha \mathrm{N}(H_E)\,H_E\,\mathrm{d}H_E = \alpha S \qquad (12)$$

where S is the collective effective dose equivalent received by the exposed population, *i.e.*

$$S = \int_0^{H_E^{\mathrm{Max}}} \mathrm{N}(H_E)\,H_E\,\mathrm{d}H_E = \sum_{i=1}^{M} H_E^i \qquad (13)$$

where M is the number of exposed individuals and H_E^i is the effective dose equivalent received by individual i. This derivation, which is somewhat different from that usually given, emphasises the interpretation of α as a quantity related to the monetary cost associated with individual exposure, or individual risk, and not, primarily, to the total collective dose to, or predicted number of effects in, the exposed population.

Thus, finally, under these assumptions, cost-benefit analysis reduces to the solution of the equation:

$$\left.\frac{\mathrm{d}X}{\mathrm{d}w}\right|_{w^*} = -\alpha \left.\frac{\mathrm{d}S}{\mathrm{d}w}\right|_{w^*} \qquad (14)$$

Since both X and S are, in principle, either measurable or calculable, this expression can be used in optimisation, though it is still necessary to select a value of α (see IAEA, 1985).

PROTECTION OF THE PATIENT

The discussion so far has related primarily to protection of radiation workers and members of the public. Intentional exposures of patients for diagnostic and therapeutic purposes and exposures resulting from the artificial replacement of body organs or functions are, in general, subject to most of the Commission's system of dose limitation. Thus, unnecessary exposures should be avoided, necessary exposures should be justifiable in terms of benefits that would not otherwise have been received, and the doses actually administered should be limited to the minimum amount consistent with the medical benefit to the individual patient. However, since the individual receiving the exposure is the direct recipient of the benefit, it is not appropriate to apply the quantitative values of the Commission's recommended dose-equivalent limits (ICRP, 1977a; see also ICRP, 1982).

In limiting doses to the minimum amount consistent with the medical benefit to the individual patient, considerations of optimisation may again be applicable. However, in the case of diagnosis, the trade-off may involve not only the monetary cost and radiation risk associated with the procedure, but also the amount of information derived from the examination and its value in diagnosis. Thus, for example, reductions in radiation exposure may be associated with reductions in the spatial or temporal resolution of the results of the procedure.

In radiation therapy, protection of the patient requires, uniquely, not the avoidance of radiation exposure or even the avoidance of risk of severe damage to some tissues. Rather, it involves achieving the optimal balance between the efficacy of irradiation in achieving sterilisation of the malignant growth and the production of the minimum of treatment-related complications. The latter involves making unwanted radiation doses as low as is reasonably achievable. The task of protecting the patient in the broader sense includes the need for proper medical training, sound clinical judgment, proper design and use of radiation-producing equipment and protective materials by properly trained staff, and careful recording of the results of treatment so that future patients can be treated even better (ICRP, 1985b).

CONSIDERATIONS FOR THE FUTURE

Clearly, any revision of the Commission's basic recommendations must take into account the most recent evaluations of data on the biological effects of ionising radiations in man. Since 1977, three areas in particular have been identified as requiring consideration. These are: the implications of revised dose estimates for survivors of the atomic-bomb explosions at Hiroshima and Nagasaki (Kerr, 1981); the recognition that *in-utero* exposure is associated with substantial risks of severe mental retardation and with a shift in the intelligence quotient distribution for the whole exposed population (ICRP, 1984a; Otake & Schull, 1984; Schull & Otake, 1985); and the methods by which exposure of the skin should be limited, especially in the context of highly non-uniform exposures.

In addition, at a conceptual level, it may be appropriate to consider whether the Commission should continue to base its recommendations on the risks of fatal cancer and serious hereditary disease, or whether it should take all the deleterious effects of radiation into account in some composite index of harm. Some preliminary consideration was given to this topic in 1977 (ICRP, 1977b) and, more recently, a much more extensive discussion of quantitative bases for developing an index of harm has been published (ICRP, 1985c).

Notwithstanding these various considerations, there is much to be said for a stable system of dose limitation. For this reason, the implications of new data and new approaches to radiation protection would have to be substantial before any change to the recommendations outlined herein would be justified.

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Practical implementation of ICRP recommendations*

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Abstract

This paper describes how the recommendations of the International Commission on Radiological Protection (ICRP) are transmitted to the government of the UK and the scrutiny which they undergo in that process. The essential features of any legislation, namely clarity and enforceability, are identified, as is the part played by consultation with persons affected. The practical outcome in terms of regulations and codes of practice is described in general terms and specific examples are taken from the regulations and codes, showing how the principal aspects of ICRP recommendations bearing on radiation risks have been incorporated. It is argued that the value of ICRP recommendations to the drafter of legislation is their general acceptability, giving a firm basis for requirements, against which too frequent and too positive detailed recommendations provide an unfortunate offset.

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Practical implementation of ICRP recommendations

Paragraph 5 of International Commission on Radiological Protection (ICRP) Publication 26 makes a number of points which are highly relevant when considering how any of ICRP's recommendations may be applied in practice. The paragraph recognises that national, multinational or international regulations or codes will be prepared based on ICRP recommendations, and that these regulations or codes should reflect local needs and practices; hence, ICRP argues that its recommendations are flexible to accommodate these. The penultimate sentence of paragraph 5 is worth quoting: "the form in which the recommendations are worded will not necessarily be suitable, and may often be inappropriate, for direct assimilation into regulations or codes of practice". That means that ICRP recommendations need in some way to be translated into some other words before they can be implemented. The end product will include instructions to workers, as well as criteria for designers and suppliers. Therefore it can be expected that recommendations which bear upon work activities will take the form of local rules or written systems of work backed up by the normal forces of management disciplines.

The final step of implementation, of course, is to get the work done and we should not forget that this is the object of the exercise. However, for the purposes of this paper it will be assumed that ICRP recommendations may be considered to be implemented when the worker has been instructed and the facilities have been provided. It will therefore focus on the intermediate steps between the published ICRP recommendations and the issue of local rules or specifications for facilities.

FORMULATION OF RADIATION SAFETY LEGISLATION

The task facing the legislator in this topic is not confined to taking ICRP publications and converting them into law. Indeed, with 47 publications, of which some have been overtaken and the content of others is unsuitable or inappropriate for legislative action, that would be impossible. Some sort of sieve must be applied to identify which of the many individual recommendations should be built into legislation. It is, therefore, helpful that the pronouncements of international and multinational bodies are intermediary between ICRP recommendations and national legislation. The International Atomic Energy Agency (IAEA) commends to member states and makes compulsory for its own operations its Basic Safety Standards (IAEA, 1982). The Standards are certainly consistent with the principal ICRP recommendations.

Interestingly, the Standards are formulated in two parts, the first being regulatory in character and the second more akin to guidance. This approach has similarities with the regulation/approved code construction of the UK legislative package. Although the IAEA Basic Standards are not binding on member states, the provisions of the Euratom Directives (Euratom, 1980, 1984) are binding to the extent of the result to be achieved, the choice and method being left to member states.

The provisions of the Directives reflect ICRP principles faithfully, and not surprisingly since the input to the Directives comes from an advisory committee whose membership is in the event from European participants in ICRP deliberations. Most importantly, the Directives set a deadline for implementation by member states (April 6, 1986) and that provided considerable impetus to making the Ionising Radiations Regulations last year.

Safety legislation in this country today is formulated by consensus, with the two sides of industry presenting their views and the drafter of legislation seeking out common ground. A further vital element in safety legislation will always be its enforceability; hence, the views of enforcing authorities can and do influence the words, style and content of legislation.

The Health and Safety at Work Act formalised the procedures in that it set up a Health and Safety Commission representing both sides of industry and local authorities, with power to make recommendations for safety legislation to the Secretary of State. In practice, the proposals for the legislation are put together by the Health and Safety Executive (HSE). The Commission is required to consult government departments and other bodies that appear to be appropriate once proposals have been formulated, and wishes to see that the comments have been properly considered (indeed, they must agree the final draft version) before those proposals go forward to the Secretary of State. In particular, the views of the National Radiological Protection Board (NRPB) must be sought on all legislation bearing upon radiological protection.

Necessarily, consultation takes time, the assembly and collation of comments takes further time and the final step of analysing comments, incorporating valid ones and justifying the leaving out of others is even more time consuming. In the case of the Ionising Radiations Regulations, two distinct formal consultation exercises were undertaken; the first in 1979 was followed by the consideration of comments received by a Technical Working Party composed of representatives from both sides of industry and technical experts.

Following their considerations a Second Consultative Document was published in 1983 which contained draft regulations and draft code material. The comments received as a result of this exercise were reviewed "in-house" in the Executive and draft regulations and draft codes circulated informally on a long mailing list to the principal interested parties.

The outcome of this work was submitted to the Health and Safety Commission early in 1985; they in turn submitted the proposals to the Secretary of State in mid-1985. The Regulations came into force on January 1, 1986.

INPUTS TO CONTENT OF IONISING RADIATIONS REGULATIONS 1985

As already indicated, not all ICRP recommendations will find their way into legislation, but legislation will also necessarily contain additional requirements as a result of other inputs and pressures on the legislators. Principal among these will be the fact that the regulations are in the context of the Health and Safety at Work Act and therefore generalised provisions of the Act may be expected to reappear in a form specific to ionising radiation. Another factor which had a marked effect on the style, form and content of the regulations was the need to make the regulations enforceable, *i.e* to have identifiable, preferably quantifiable, criteria which, if met, demonstrate compliance. The criteria must be such as to be readily capable of assessment by employers, employees and inspectors.

To show the extent to which the regulations reflect ICRP recommendations, particularly those of ICRP 26, one can look at Parts F and G of ICRP 26 which purport to give general guidance on the application of ICRP recommendations. In fact, there is only one significant difference between the regulations and ICRP recommendations, and that occurs in the provision relating to controlled areas. If one looks at other ICRP documents one can find many "sins of omission", but it is doubtful if there are too many "sins of commission", *i.e.* provisions where United Kingdom legislation has taken a totally opposite line.

PRINCIPAL ICRP RECOMMENDATIONS AS INCORPORATED INTO UK LEGISLATION

(a) Justification

Other than brief mention in the preface to the Approved Code of Practice, the regulations do not address themselves to the issue of justification. Firstly, because the question of justification of a practice is handled in the UK by other means, such as planning enquiries for matters like nuclear reactor or nuclear fuel processing, and secondly because the Health and Safety at Work Act contains the power to prohibit (by regulation) any specified activity. Thus, if it were felt necessary to prohibit the use of fluoroscopy as an aid to shoe fitting it would be necessary to draft an appropriate regulation, consult (as for any other Health and Safety regulations) and then submit the proposal to the Secretary of State.

(b) Limitation

The ICRP recommends numerical values for dose limits. These same values appear in the regulations as absolute requirements, that is, any excess of dose above the dose limit, prima facie, creates an offence. The duty to observe the legal requirements falls, in general, to the employer of the worker concerned. Throughout the development of the regulations there was pressure from various groups and individuals to set lower dose limits than those of ICRP; this course was not followed: the UK Government position is that in setting dose limits advice is sought from NRPB and that advice has consistently been to follow ICRP Standards.

(c) Optimisation

The bulk of the regulations and Approved Code is about keeping doses as low as reasonably practicable. The Code in many cases actually indicates what is thought to be reasonably practicable in particular circumstances. For the purposes of this paper, it is not necessary to distinguish between the ICRP wording: "as low as reasonably achievable" and the regulatory wording: "as low as reasonably practicable". In practical terms these phrases have the same effect, that is, of looking critically at the doses involved in a particular operation in the light of the cost, whether in time, trouble or money, of reducing those doses and the benefit of so doing. The regulations do not require any particular way of carrying out that exercise any more than ICRP does.

SECTIONS F AND G OF ICRP 26

Turning now to look at some of the recommendations of Sections F and G of ICRP 26 to see how they compare with the regulatory requirements, Paragraph 38 suggests that professional judgement is called for in the application of all ICRP recommendations This is achieved in part by the considerable amount of professional judgement which went into the formulation of the regulations anyway. On a day-to-day basis the professional judgement input is provided by the Radiation Protection Adviser (RPA). He is required to be appointed by the employer for the purpose of advising him as to the observance of the regulations and as to other health and safety matters in connection with ionising radiation.

The Code, at Paragraph 71, lists in general terms the substantial amount of qualifications, experience and qualities which the RPA should possess and particularly attention is drawn to the last in the list, namely "an appreciation of his own limitations whether of knowledge, experience, facilities or resources".

Paragraphs 140–142 of ICRP 26 point out the need for the pre-planning and prior assessment of facilities, together with predictive assessment of likely doses. Two regulations, 32 and 25, are particularly relevant here. Regulation 32 places duties on manufacturers, suppliers, etc., of articles for use at work to ensure that the article is designed and constructed to restrict, as far as reasonably practicable, the extent to which persons are likely to be exposed to ionising radiation. The regulation goes on to require, where the article is erected or installed, that a critical examination of the way in which the article was installed shall take place and the Radiation Protection Adviser should be involved. Thus, we can expect proper installation of equipment and thorough commissioning surveys and assessments.

Regulation 25 requires all employers to look at the work which they propose to do and identify potential hazards. There is then a duty, where reasonably practicable, to eliminate or limit such hazards and to instruct employees on how to deal with them.

Paragraphs 149–152 of ICRP 26 describe the ICRP system of reference levels. These are formulated in Regulations 13(3)(f) and 28 into the upper and lower enquiry levels. The upper level requires a special report to the HSE whenever any worker exceeds 3/5 of the annual dose limit in any calendar quarter. The lower level is set at 3/10 of the annual limit in any calendar year where it is required that the employer conducts an investigation with the objective of determining whether the doses are being kept as low as reasonably practicable.

Clearly, the very existence of formal enquiry levels will do much to provide an incentive to employers to devise ways of keeping doses as low as reasonably practicable and, in any event, below the enquiry level. The setting of the lower enquiry level is such that employers may well have the added bonus of avoiding classification of their workers if they set out to keep below it.

Operational optimisation is discussed in Paragraphs 153–159 of ICRP 26. Essentially, the whole of Part 2 of the Code is about operational optimisation in the various sectors of work involving ionising radiation.

In Paragraphs 161 and 162, ICRP identifies a "Working Condition A" in which workers should be subject to special radiological and medical supervision. In this area the regulations have, of necessity, to be more formal in order to achieve accurate and enforceable identification of classified workers. This is met by the requirement that only classified persons (or persons entering under a restrictive written system of work) may enter a controlled area.

Controlled areas are also dealt with in these paragraphs (161, 162) and the corresponding regulatory requirements are contained in Regulation 8 and Schedule 6. Here there is a difference from ICRP in that Paragraph 165 says the "classification of areas takes no account of the time spent by workers in the area during the course of the year" whereas occupancy of areas is a factor which may be taken into account in classifying areas under the regulations (see Paragraph 3(c) of Schedule 6).

The monitoring and dosimetry requirements of Paragraphs 173–183 are carried into legislation by Regulations 24 and 13, which deal with workplace monitoring and personal dosimetry, respectively. Likewise, the medical surveillance recommendations of Paragraphs 184–187 are paralleled by Regulation 16 and Code Paragraphs 100–102.

Finally in this brief review of corresponding provisions, ICRP 26, Paragraphs 188–194, deals with intervention in abnormal situations. Four regulations are needed to cover this ground: 14, 27, 29 and 31. Essentially, these require that contingency plans be devised by all employers against foreseeable incidents and that individual exposures greater than the dose limit be investigated and reported to the Health & Safety Executive.

CONCLUSION

ICRP 26 recommendations have been implemented by the Ionising Radiations Regulations, 1985, certainly in spirit if not entirely in detail. No doubt one could identify recommendations in other ICRP publications which have not been incorporated into regulations or codes. These may appear, of course, in guidance material yet to be published, even supposing the essential intermediate step of preparing and agreeing a Euratom Directive could have been completed more quickly. Minor changes may be able to be executed rather more speedily but it is doubtful whether the UK would act to implement minor ICRP changes ahead of an amendment to the Euratom Directive.

All legislators in the safety field hope that their legislation will remain unchanged for at least a decade. Frequent minor changes are very difficult to deal with and lead to a diversion of resources from other tasks, such as the preparation of supporting guidance material.

It follows, therefore, that minor recommendations emanating every year from the meetings of the International Commission on Radiological Protection are not always welcomed by legislators in the way they should be, although the corresponding changes to Directives do in the event provide a welcome cushion.

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Radiation risks in perspective

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ABSTRACT

The main difficulty in presenting radiation risks in their proper perspective is that they must, in most cases, be estimated predictively. This contrasts with most other occupational and public risks, of which the magnitude and severity are known from past records and experience. The problem is greater at the low effective dose rates now observed in the majority of all forms of exposure, usually of less than 3 mSv per year from natural causes, from occupational exposure, and from exposure of "critical groups" of the general public. For most of these populations there are particular problems also in epidemiological studies at low dose, in addition to those due to the very large numbers of person-years that need to be studied and the long latencies of most radiation effects. Adequate estimates can, however, now be made of the carcinogenic risk of exposure at higher dose of various organs selectively and of the whole body uniformly, and of modes of inference to the risk at lower dose. Estimates can also be made of the risks of inducing major types of inheritable and developmental abnormality. An essential step in viewing the sum of all such radiation risks in the perspective of other occupational and public risks must now be to develop an informed consensus on the relative weight that is regarded as attaching to hazards of different kind and severity.

ESTIMATION OF RISK RATES

For many kinds of occupational risk, and for some kinds of public risk, records have been maintained for several decades which show the rate at which various types of harmful effect occur in different industries or conditions and in different countries. The magnitude of these risks, and their trends with time, can therefore be estimated, and a clear perspective can be obtained, for example, on the differences in the risk of accidental death at work in different industries or occupations (International Commission on Radiological Protection (ICRP), 1985).

For agents such as ionising radiation or certain chemicals, of which any carcinogenic or mutagenic effects may continue to be expressed for many years or decades after exposure, available records of past experience may be inadequate to assess the risk of present exposures. This is particularly true for low levels of exposure, if small numbers of induced cancers or inherited defects would need to be discriminated from much larger numbers of identical abnormalities which would have occurred naturally, in the absence of such exposure.

In some instances, admittedly, a clearly increased mortality from certain types of cancer has been recorded in occupations involving exposure to agents such as nickel, asbestos, beta-naphthylamine or mustard gas. In such cases, numerical estimates can be made of the lifetime or annual risk of fatal cancer induction by previous occupational exposure (Doll & Peto, 1985; ICRP, 1985), and particularly when exposure levels had been high, or an unusual type of cancer was induced. Similarly, estimates can be made of the risk of bone sarcoma from radium ingestion in early dial painters (Martland, 1931), and of lung cancer in underground hard rock miners who had received substantial exposure from radon and thoron daughter products and from gamma radiation at work (Myers & Johnson, 1984).

In general, however, estimates of the risk of most present forms of occupational and public exposure to radiation must be predictive, rather than based directly upon recorded experience. This is unavoidable in view of the low dose rates now observed in most occupations, and in locally or regionally exposed members of the public; and because of the statistical problems involved in deriving any reliable risk estimates from exposures at such low dose rates

DOSE RATES CURRENTLY RECORDED

Mean dose rates are now less than 3 mSv per year in a majority of occupations involving radiation exposure: in 19 out of 23 reported for 1980 in the USA (Kumazawa et al, 1984), in 12 out of 16 occupations in 1980–82 in the UK (Hughes & Roberts, 1984), and in 10 out of 14 of the average values, for about 1978, for countries reported by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1982).

While annual doses are substantially higher in a few occupations, mean doses of external radiation from occupational exposure thus appear to be comparable with effective dose equivalents from natural sources. For most countries these natural doses are estimated as about 2 mSv per year (UNSCEAR, 1982), about half of the effective dose being due to lung irradiation by radon daughters, although in some localities the latter component raises the annual effective dose to values similar to those recorded for some forms of hard rock mining.

The exposures of local groups of members of the public, as a result of liquid discharges from nuclear establishments, are in most cases substantially less than those from natural sources. Thus the annual doses (the committed effective dose equivalents) received in 1984 (Hunt, 1985) by the 30 such critical groups identified in the UK, were less than 0.1 mSv in 20, and less than 0.5 mSv in a further nine. In one community, relying on fish and shellfish derived from areas adjacent to the pipeline discharging from the nuclear fuel reprocessing plant at Sellafield in Cumbria, the estimated dose was 0.84 mSv, but would have been 2.0 mSv if mollusc consumption had been at the 1983 rate (Environment Committee of the House of Commons, 1986).

DETECTION OF CANCER RISK AT LOW DOSE

The difficulties in obtaining any valid estimate of total carcinogenic risk from populations exposed at dose rates of a few millisieverts per year or less, result from the very large numbers of person-years that need to be reviewed, and the necessity for equally large or larger comparison groups of which the members had not been equally irradiated but were exactly similar in all other relevant respects. Even if the expected number of deaths from cancer were validly estimated from such a comparison group, a small excess of deaths above this number could only be reliably discriminated if it exceeded about twice the standard error by which this expected number would necessarily vary due to sampling. Moreover, to evaluate the induction rate, even approximately, the excess would need to be greater than three times this standard error. This in itself must create difficulty in evaluating any general carcinogenic effect of low doses in areas of high natural background radiation.

Detection in high background areas

The expected annual number of deaths from cancer per million of population, in populations having a long life expectancy, is about 2500 (World Health Organization (WHO), 1983). To detect a 2% increase in this rate, such as might be expected if a regional population, exposed at 4 mSv per year, were compared with a large population of more normal exposure of 2 mSv per year, would require a regional study comprising about 4 million person-years to establish the presence of an excess reliably (since $4 \times 2\%$ of $2500 = 2\sqrt{4 \times 2500}$); or over 9 million person-years to determine its size at all accurately (since $9 \times 2\%$ of $2500 = 3\sqrt{9 \times 2500}$). In countries with a shorter mean life expectancy, annual cancer mortality rates per million are ordinarily lower, and the size of studies required would be correspondingly higher. For example, with an expected rate of $1600\ 10^{-6}\ \text{year}^{-1}$, the sizes of study for detection, or for determining the size, of a 2% increase would be 6.2 million and over 14.0 million person-years, respectively. The scale of any such surveys would, in itself, increase the difficulty in ensuring exact comparability between the populations in areas of high and low background dose, in respect of all factors other than radiation which may affect cancer mortality.

The difficulties might be less, although still substantial, in detecting the induction rate of individual cancers in populations exposed at low dose rates, if the statistical penalties of relying on smaller numbers of cancers were offset by a greater induction of a particular cancer relative to its normal incidence (Pochin, 1984). Similarly, an excess might be more readily detectable in a group of restricted age and sex than in the total population. In general, however, the limiting consideration must be the prohibitively large surveys required for direct evaluation of cancer induction at very low doses, given that the necessary size of survey increases about in proportion to the inverse square of the dose to which the studied population has been exposed.

Detection following occupational exposure

The direct evaluation of carcinogenic risks of occupational exposure at low dose rate is further complicated by the "healthy worker" effect (Fox & Collier, 1976; Checkoway et al, 1985; Weed, 1985), rendering comparisons between disease rates in a working population and in the general population invalid. It is, moreover, clear, if perhaps surprising, that the differences may affect even cancer mortality rates for many years after recruitment into industry (Fox & Collier, 1976), although less strongly and for rather less long than may apply to other diseases. The consequent need, to compare cancer rates in groups of workers exposed at different dose rates within the same industry, involves a reduction in numbers in the groups on which any risk estimates can be based, as well as a presumption that work at different dose rates does not imply different kinds of work and therefore different medical selection pressures at recruitment. If, however, a relationship between cancer risk and dose is established in this way, the evidence is obviously very much stronger that an excess of cancers is due to the exposure rather than to some other factor generally present in the working environment.

Studies that have been reported hitherto, however, are too limited in numbers to give any clear indication of the size of whatever carcinogenic risk may be involved. The Hanford investigations concerned 21800 persons potentially at risk, amongst whom 5340 deaths had occurred, 1123 (23%) of them from cancer (Kneale et al, 1981, 1984). A total in the order of 10 deaths from induced cancer might ultimately be expected to result from the collective dose (from external radiation, of 737 person-sieverts) hitherto recorded. Even if this number of deaths had already occurred, it would not be reliably identified within the present 1123 deaths from cancer. Multiple myeloma remains as the one malignancy in which the three deaths in those exposed (at over 0.15 Sv) substantially exceeds the number expected on the basis of rates in the unexposed (Tolley et al, 1983). This excess would be highly significant ($p = 0.006$; Gilbert & Marks, 1980) if viewed in isolation but, when recorded as the excess for the malignancy with the highest relative risk of the 15 cancers recorded, is of more doubtful significance, with $p = 0.09$, since

$$(1-0.006)^{15} = (1-0.09)$$

The evidence from a study of Atomic Energy Research Establishment workers, including 20382 with occupational dose records, is similarly still inadequate to yield any accurate carcinogenic risk estimate (Beral et al, 1985). In those with dose records 1789 deaths are reported, 473 of them from malignant disease, following a collective dose of 660 person-sieverts. An excess mortality rate from all cancers was estimated as 1.25 deaths per million person-years and per millisievert, but this value did not differ significantly from zero, its 95% confidence interval ranging from a *reduction* of cancer mortality by 2.2 deaths, to an increase by 5.2 deaths, per 10^6 person-year-millisieverts. In the case of one cancer, that of the prostate, the mortality rate correlated with the cumulative dose (of external radiation) recorded, with 14 deaths in those exposed at over 10 mSv, and 11 deaths after less than 10 mSv. Taken in isolation, the association with dose was highly significant, at $p < 0.001$; or, as the highest association among 15 cancers recorded, p is still likely to be less than 0.015.

It is obviously most important that such studies should be continued over longer periods and involving larger groups of occupationally exposed workers, as are now being studied in several countries (*e.g.* National Radiological Protection Board (NRPB), 1985) to determine within closer limits the value of such risks of fatal cancer induction as may result from occupational exposure at low dose rates.

Detection in small communities

In interpreting the significance of cancer rates observed in small communities, or at particular ages in these communities, the problems of selecting valid comparison groups may be great, even though those imposed by the small numbers involved are usually greater. The known variations in cancer incidence or mortality with years of survey and with age and sex distribution of the populations are readily allowed for in any competent epidemiological survey. The known variation of cancer rates with locality, in the absence of identifiable radiation or other causes, however, may present greater difficulties, as may the variations with professional or "social" class, and with local differences in reliability of leukaemia and other cancer diagnosis or registration, and their trends with time in different regions.

Above all, however, considerable problems (and misunderstandings) result from the much greater variability of small numbers, *e g.* of cancers observed or expected in a limited age group in a small community or group of villages, than in the larger numbers based on surveys of larger areas.

If, for example, an average of three such deaths were to be expected in any community of 4000 people of all ages during a stated period of time, as estimated on the basis of national statistics and ignoring causes of local variation, chance alone could cause the number actually observed to vary between 0 and 12 if communities of equal size throughout the UK were examined. This range would be predicted from the numbers corresponding to successive terms of the expansion of e^3, according to a simple Poisson distribution, and with $56 \times 10^6/4 \times 10^3 = 14000$ communities of equal size throughout the country (Table I). Factors such as a variation in size of individual communities would be likely to increase the range, for example to one of from 0 to about 20 in a "modified Poisson distribution" (Kendall & Stuart, 1977; Swansbury, 1985) for which the variance had twice the mean value of 3.

TABLE I

If a total population of 56 million were subdivided into 14000 equal subpopulations of 4000, each with the *same* expectation of 3.0 cases in a given period of time, a simple Poisson distribution (by expansion of e^3) would predict an expectation of

470 of the subpopulations having 7 or more cases
15 of the subpopulations having 10 or more cases
1 of the subpopulations having 12 or more cases

This hypothetical example illustrates the difficulties which must arise in interpreting malignancy rates in small communities which are reported without adequate reference to, or evaluation of, the normal variability of small numbers in multiple samples (Smith, 1982). Moreover, when increased numbers of cancer deaths are found in small communities suspected of raised local levels of ionising radiation or other carcinogen, it is rightly emphasised that an excess may not be detectable if mortalities are examined in larger areas which include these communities. It is pointed out that a supposed effect may be "diluted" and no longer significant, owing to inclusion of data from larger surrounding and unexposed populations It is not always appreciated, however, that an exactly similar effect would occur when larger populations were examined, if the raised values in the small community had been random rather than significant. Under the same assumptions of an expected number of three cases per 4000 of population in a defined number of years, Table II indicates the decreasing proportional variability of cases expected in survey areas of increasing size, again assuming a simple Poisson distribution.

It is, I think, evident therefore that the need is not simply for the comparison of findings in small communities with national averages, but for much more comprehensive surveys of the variability of malignancy or other rates in such small communities in general, with proper recognition of factors such as age, sex, time period, "social class" and efficiency of recording, which are known to influence malignancy rates, both of

TABLE II

EFFECT OF SIZE AND NUMBER OF SUBPOPULATIONS

Size of each subpopulation	No. of subpopulations (in total population of 56 million)	*Average* no. of cases per subpopulation	*Max.* no. of cases in any one subpopulation	Ratio (max. number/ average number)
4000	14 000	3	⩾ 12*	⩾ 4.0
8000	7000	6	⩾ 17	⩾ 2.8
16 000	3500	12	⩾ 26	⩾ 2.2
40 000	1400	30	⩾ 49	⩾ 1.6

**i.e.*, with one of the 14 000 subpopulations likely to have 12 or more cases etc.

incidence and of mortality, in different areas and populations.

Such wider surveys should properly eliminate a potential source of bias which may arise also in the selective reporting of abnormal risks in areas suspected *a priori* of being at risk. When rates of any abnormality in small communities depend critically upon the inclusion of small numbers of cases, bias can very easily result from any selective inclusion, or exclusion, of individual cases, as a result of the criteria adopted for estimating the number of abnormalities. Given the great variability of any one rate depending on small numbers of cases, there is obviously a large chance of apparent significance when so many alternative rates, even of the occurrence of malignancies, can be examined and may be reported. The rate reported as abnormal may be in the incidence or the mortality of cancer, or of any one form or group of cancers, over any time period, in any age group or in either sex, or at any defined distance from a nuclear plant. Gross bias may obviously occur if, for example, the boundaries of the areas studied are set with knowledge of the geographical position in which individual cases occurred. With so many relevant degrees of freedom and possibilities of bias involved in the choice of criteria, the need for properly conducted and extensive epidemiological surveys becomes both greater and more arduous, and the value of selective reports on single communities becomes correspondingly less.

It remains true, therefore, that reliable estimates have not yet been obtained of the ultimate risks of radiation exposure at rates of a few millisieverts per year. Approximate estimates of thyroid cancer induction at doses of the order of 100 mSv have been obtained by the study of rather over 10 000 individuals so exposed in childhood (Ron & Modan, 1984); and of malignancies induced in childhood following exposure of rather larger numbers, to rather lower doses, *in utero* (Stewart & Kneale, 1970). Some indication of an excess of lung cancers has been found in non-smokers exposed to moderately increased radon levels (Edling et al, 1984). At lower dose, however, the extensive surveys of all occupationally exposed workers that are in progress in several countries should at least increase the precision with which the risk of exposures received 10 and more years previously can be defined.

INFERENCE FROM RISK AT HIGH DOSE

In general, however, the risks of cancer induction at the very low annual doses now being received in most occupations and by members of the public, apart from medical exposures, must continue to be derived by inference from risks observed to follow exposures to higher doses. This is likely to be true for the totality of all cancers induced, or of those causing death, and of most individual forms of cancer, unless criteria are discovered by which radiation-induced cancers can be distinguished from cancers resulting from other causes. And the same is likely to apply to the risks of inducing inheritable abnormalities and particularly also to the induction of congenital defects by irradiation *in utero*.

With regard to carcinogenesis, Upton (1987) has discussed aspects of the large body of radiobiological evidence which increases the confidence with which the frequency of cancer induction at very low dose can be inferred from the frequency per unit dose observed at higher dose. Many of the early radiobiological studies were concerned with cell killing effects, which are likely to be relevant mainly to radiation effects at high dose, although probably important also to some aspects of the induction of developmental abnormalities. Information on the reduced efficacy of doses when protracted over long periods of time, however, is potentially of great importance, since, for example, the total doses received from natural sources during a whole lifetime, or from many occupational exposures during a working life, are comparable in size with some doses from which epidemiological risks in man can already be directly estimated when they are delivered at high dose rates over short times.

The progressive increase of RBE for some forms of high-LET radiation that may occur with decreasing dose (Commission of the European Communities (CEC), 1982) is quantitatively important also, as presumably representing the product of any increasing effectiveness per unit dose of the high-LET radiation, and a decreasing effectiveness per unit dose at low doses of the low-LET radiation with which it is compared.

The separate quantification of these two contributors to the overall increase in RBE is of obvious importance in inferring the changes in risk per unit dose of high- and low-LET radiations at increasingly low doses.

Given, however, the continuing need, and an increasing justification, for inferences based on estimated risks at higher dose, it is important to recognise both the strength, and the measures of uncertainty, involved in these estimates of risk at higher dose.

Consistency of Cancer Risk Estimates

The strength derives from the approximate consistency between the induction rates of particular types of cancer found in epidemiological surveys of populations exposed in different ways and for different reasons. If proper allowance is made for factors such as age at exposure and periods of follow-up, broadly similar risk estimates have been found for cancer mortality following treatment of ankylosing spondylitis and atomic-bomb exposure (Darby et al, 1985a), for leukaemia following bomb exposure and treatment of metropathia haemorrhagica (Darby et al, 1985b), and for breast cancer induced by radiation in different circumstances (Land et al, 1980) A detailed review was also published by UNSCEAR (1977) of the risk estimates derived from different sources, and their confidence limits, for cancer induction, particularly in thyroid, breast, lung and bone, and for leukaemia. Estimates of lung cancer mortality in different forms of hard rock mining, and of liver cancer and leukaemia following Thorotrast injections, have commonly shown reasonable consistency within their estimated confidence intervals, in surveys of exposed groups in a number of countries.

Uncertainties in Cancer Risk Assessments

We should, however, note the extent by which the carcinogenic risk estimates for some organs remain uncertain, and the ways in which these uncertainties may be being resolved.

"Absolute" or "relative" risk hypotheses

In the case of two forms of malignancy, the increased mortality following radiation exposure has greatly diminished within 30 years of the exposure. in leukaemia, following exposures such as occurred in Hiroshima and Nagasaki; and in bone sarcoma, after the short exposure of bone cells due to radium-224 injections. In these cases, the "absolute" risk can be adequately assessed by epidemiological surveys of the length that have already been made.

For several other forms of malignancy, present evidence strongly suggests that induced cancers will continue to develop for longer periods after the exposure, and perhaps during the whole remaining lifetime. Moreover, for some organs, and particularly for the female breast, the induced cancers appear to become detectable at the ages at which cancers of the organ normally develop. In these cases, the effect of radiation exposure appears to be that, after an "absolute" latency of 10 or fewer years, the natural incidence of the cancer is increased by a constant proportion during the periods so far surveyed (Committee on the Biological Effects of Ionizing Radiation (BEIR), 1980).

An important assessment of the recent evidence on this subject (National Institutes of Health (NIH), 1985) regards the absolute risk model as applicable to leukaemia and bone, and a relative risk model as indicated for breast, stomach and probably lung, although for lung the evidence is shown to be equivocal. For the seven other organs for which risk estimates are quoted (oesophagus, colon, liver, thyroid, salivary glands, kidney and bladder, and pancreas) it indicates that there is no adequate evidence to discriminate between the two models, but opts for use of the relative risk model in estimating a variation with age of tumour expression following exposure.

The latest study of the Japanese Life Span Study populations (Preston et al, 1987) advances the position somewhat by reporting that, for thyroid cancer, "the relative risk seems to decrease with time for all . . . groups" exposed at different ages. In other cancers also, the value of the relative risk appears to vary with time since exposure.

The report also states that "the results of analyses with (preliminary estimates of the revised doses) suggest that (a) there is virtually no difference in the dose response for the two cities; (b) relative and absolute excess risk estimates based on new exposure dose are expected to be about one and a half times the corresponding (previous) T65DR risk estimates".

Although it remains uncertain, therefore, for how long and in what way cancers of different organs will continue to appear following radiation exposure, the estimated differences in number of induced cancer deaths to be expected according to the alternative models are not considerable This is probably because the possible excesses predicted for older ages by a relative risk model, but absent acording to an absolute risk model, are subject to increasingly dominant competing causes of death at these older ages (Dunster, 1986). The "BEIR III" report (BEIR, 1980) derived estimates for total numbers of deaths from all induced malignancies according to the two models following continuous annual exposure at a constant rate for the whole of life, or for the whole of working life (ages 20–65 years). In the case of lifelong exposure, the relative risk model was estimated to predict 2.5 times as many deaths as the absolute risk model. For continuous exposure during working life, the ratio would be 1.7. These ratios may somewhat overestimate the uncertainty, in view of the evidence obtained in the Radiation Effects Research Foundation (RERF) report (Preston et al, 1987) mentioned above, which now includes cancer mortalities up to the end of 1982, *i.e* to just over 37 years from exposure.

The NIH report (NIH, 1985) is valuable also in summarising current informed opinion on several other factors influencing risk estimate for cancer induction in individual organs: such as the variation in risk according to the age at exposure, or to the sex. The latest RERF report (Preston et al, 1987) also extends the evidence on sex differences in induction rate, whether assessed in absolute or in relative terms. The more probable dose–response models for cancer induction by low-LET radiation are also discussed in the NIH report, suggesting a linear relationship as the more likely for human thyroid and breast cancer induction, and a linear quadratic model more likely for the remaining nine types of malignancy assessed.

Risk of cancer mortality and of total incidence

Many of these assessments refer only to risks of death from induced malignancies, comprehensive records of all deaths from cancer being more consistently obtainable than the records of all operations or other forms of effective treatment for cancer over the long periods that would be needed to determine total cancer incidence reliably in exposed communities. It is likely, however, that radiation-induced cancers behave in the same way clinically as naturally occurring cancers of the same histological types. For organs in which the fatal cancer induction rate can be estimated, therefore, it is likely that the total induction rate, of fatal and curable cancers, can be reliably inferred from the known induction rate of fatal cancers and from at least the long-term survival after treatment of naturally occurring cancers of the same types (ICRP, 1985). For some tissues it is necessary to take account of the types of cancer induced by ionising radiation (*e.g.* of leukaemia excluding the chronic lymphatic type; of skin probably excluding malignant melanomas; and of thyroid apparently excluding the medullary and, at least usually, the anaplastic cancers). For most organs in which selective concentration of radionuclides is likely to occur, and for uniform whole-body exposure, it appears reasonable to infer total induction rates from available estimates of induction of fatal cancer on this basis.

Total induction of malignancies

A final area in which more analysis is needed, however, is the mode of inference from risk estimates for the individual organs or tissues for which such estimates can be made, to the total for all organs irradiated. It seems unlikely that, with the latest RERF survey already extending to 37 years from exposure, any large excess will now emerge from tumours of uniformly long latency of development. At the same time, the total rate is likely to be biased if it is based upon the sum of the rates estimated for individual organs. For some organs, a small induction rate may not have been detected, particularly if the natural incidence is high. For others, rates will have been estimated with wide confidence intervals, but will probably have been reported only if lying within the upper part of this range of uncertainty.

A more reliable estimate is likely to come from the conjunction of two pieces of information: firstly, the ratio between the total excess of all fatal malignancies other than leukaemia, and the total excess of deaths from leukaemia, in populations studied for a long period after whole-body exposure; and secondly, existing estimates of the leukaemia induction rate per unit dose.

The latter figure can now be based on a number of independent epidemiological surveys yielding reasonably consistent estimates. Moreover, the reduction of any increased mortality almost to zero by 30 years after exposure suggests that the total risk will have been recorded within such a period.

The ratio of deaths from induced malignancies other than leukaemia to those from leukaemia rises with time after the cessation of excess leukaemia deaths. At the end of 1982 it stood at about three in the augmented Life Span Study populations exposed in Hiroshima and Nagasaki (Preston et al, 1987). This still represents only 37 years from exposure (excluding the first 5 years, during which no solid cancers and probably few leukaemias will have occurred or caused death) in a population of mean age 30 years at the time of exposure. The data available from this survey, however, should yield estimates of the level to which this ratio would ultimately rise after continuing exposure.

Thus, the report records the excess numbers of deaths, both from leukaemia and from all other malignancies, which occurred in each successive 4-year period since 1950. It gives these numbers separately for those exposed at different ages (from 0 to 9, 10 to 19, 20 to 34, 35 to 49, and 50 or more years of age). Moreover, for each age group at exposure, data are given on the number of cancer deaths occurring specifically at subsequent attained ages (by 10-year age intervals). At least an approximate estimate should, therefore, be obtainable for the ultimate value that would be reached by this ratio of induced other cancers and leukaemia, and hence a risk estimate for total malignancies induced per unit dose by this form of exposure. This total risk would include the aggregate of all individual cancers, regardless of the reliability of their separate determination, and regardless of whether an absolute, a relative, or any other model applied to the time course of their appearance after exposure.

It can, I think, be concluded, therefore, that reliable quantitative information is available or becoming available from a number of sources, on which the total carcinogenic risk of radiation exposure in man can be based with reasonable confidence and accuracy, with an indication also of the variation of this risk with age at exposure, sex and time since exposure, or as a result of the selective irradiation of various major body organs. It may be noted that comparable quantitative information has been obtained on the carcinogenic risks of chrysotile asbestos fibres in the working environment

(Doll & Peto, 1985); and of tobacco smoke inhaled in active smoking or, with less consistency, in "passive" smoking. For various potentially carcinogenic chemicals, however, risk estimates have been derived only for high or prolonged exposures to the agent.

Reliability of Other Risk Estimates

With regard to other risks of radiation, it is clear (Lyon, 1987) that estimates can be obtained from various sources of the number and range of inheritable abnormalities that may be induced by a given exposure. Uncertainties necessarily remain on the relative frequency of their expression following irradiation of male or female germ cells (UNSCEAR, 1982), on the importance of "recessive" mutants, and of conditions with multifactorial determination; and also on the quantitative application to man of relevant aspects of mouse genetics, although the continuing study of protein variants in the children of atomic-bomb survivors may ultimately throw more light on radiation-induced mutation rates in man.

In the causation also of developmental abnormalities, quantitative risk estimates have become possible for the frequency with which mental retardation (Otake & Schull, 1984) or lesser degrees of mental impairment (Schull & Otake, 1985) may be induced by exposures *in utero* (Mole, 1987). The data from Hiroshima and Nagasaki give no indication of a threshold for induction of severe mental retardation, but these data rest on the induction of such retardations in rather few children, and a threshold even of several tens of millisieverts is not excluded statistically. This is important because, in typical occupations involving dose rates of only a few millisieverts per year, if received at a regular rate, the embryo would be likely to receive less than one millisievert during the 8-week period in which the dose–effect relationship appears linear with possible absence of a threshold. The damage would, therefore, be excluded by the existence of a threshold which was much smaller than that ordinarily assumed for other developmental effects which depend on multiple cell killing. It seems important, therefore, to confirm the cellular mechanism of the effect, and to extend if possible the statistical evidence for its induction. In protection practice, however, for an effect which may depend on the malfunction or death of very few glial cells during a period of neuronal migration, it seems appropriate to treat the possible induction of mental retardation as a stochastic effect which may be induced without threshold, and to take the estimated magnitude of the risk into account in just the same way as that of leukaemia induction in the developing child would be taken into account, as a stochastic phenomenon liable to be induced without threshold during development *in utero*.

Perspective

It gives, I believe, a very necessary perspective to have some comprehensive, even if only approximate, numerical estimate of the various risks of radiation exposure at low or moderate dose. To comprehend this perspective, however, needs a deeper insight. The word "perspective" normally refers to the way in which we see, and should depict, objects in relation to other surrounding objects. The laws of visual perspective are partly geometrical. The depiction of objects in perspective, however, also involves a proper use of colour, tint and shadow to indicate their relationship to their background and surroundings.

In much the same way, the risks of radiation exposure cannot be put into their proper perspective with other surrounding risks only by a numerical comparison: for example, by emphasising the equal loss of years of life expectancy due to the carcinogenic risks of occupational exposure at 2 mSv per year and that due to an annual accidental death rate at work of 2 per 100 000 exposed (ICRP, 1985). The numbers—the geometry of the perspective—are, I believe, a necessary component of any attempted intercomparison of dissimilar risks; but they cannot be sufficient: The differences in types of risks are as important as the sizes of the risks: the difference between an accidental death now and a distressing death from disease in 20 years time; or between chronic industrial disease and permanent disability from injury; or between disease in the exposed individual or in one of his descendants several generations later. When comparing the overall safety of occupations involving exposure to radiation, or to other carcinogens or mutagens, with the safety of a range of other conventional industries, what relative weight must be put, and what weight do people put, on different kinds of harmful effect—fatal or readily cured cancers, severe permanent injuries or immediately fatal injuries, or accidental deaths occurring early or late in life?

Intercomparison of Dissimilar Risks

It is easy, and true, to say that such dissimilar events are non-commensurable in any formal sense. We must, however, recognise the need to review the gravity of carcinogenic or genetic risks in the context of other and more familiar risks of comparable severity; and people do, in fact, choose between alternatives involving risks of different kinds and magnitudes.

It has been conventional, in many national records, to indicate the relative safety or hazard of different industries by records of the annual frequency (*e.g.* per 10^5 workers) of fatal accidents at work, of non-fatal injuries of a loosely defined severity (*e.g.* as involving more than 3 days off work) and of certain diseases recognised as being of industrial origin. ICRP has published reports (ICRP, 1977, 1985) which review the frequency of different kinds of harmful effect incurred at work in different industries and in different countries, including the likely frequency of radiation effects in occupations involving different rates and types of exposure. These reviews have indicated the total lengths of active and healthy life lost from such injuries or diseases, or of life expectancy lost as a result of them in different circumstances, in the presumption that some such measure of the loss of healthy life and activity should be one of the relevant factors in developing an informed opinion as to the weight that should properly be placed on different harmful effects. It is evident that different weight would be placed on equal durations of full health or activity lost, for example owing to a series of minor injuries, or from serious illness or permanent disability, or by loss of life expectancy from fatal injury or disease.

No realistic perspective can be expected, however, on the importance of occupational or public risks of radiation, unless both the magnitude of these risks and their perceived detriment are taken into account together and seen in relation to the full range of other risks to which the worker or the public may be exposed. Without such a full perspective, the protection and safety of the community are liable to be based on incomplete information and unbalanced criteria.

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Growing points in radiotherapy since 1930

The 65th Mackenzie Davidson Memorial Lecture 1984*

By Frank Ellis, M.A., M.Sc., M.D., F.R.C.P., F.A.C.R. (Hon.), D.M.R.†

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I feel greatly honoured in being asked to give this, the 65th Mackenzie Davidson Memorial Lecture, in honour of a Scotsman born in Buenos Aires but educated in Scotland who had the initiative and imagination, at the age of 29, the year after Röntgen's publication, to renounce an already successful career as ophthalmic surgeon and university lecturer in the medical school at Aberdeen to devote his inventive and clinical talents to radiology. He was knighted in 1912 and was the elected president of the Röntgen Society in 1912–13; he was the president of the British Association of Radiology (BAR) and the British Institute of Radiology (BIR) from 1917 to 1919, when he died at the age of 62. The title of this lecture committed me to too large a subject, but I felt that the remarkable growth of radiotherapy since 1930, when I started, should be reviewed. Hence, I aim to mention many important growing points and to discuss others more directly affecting clinical radiotherapy.

Following the recovery of King George V from pneumonia in 1929, money collected as a national thanksgiving fund for his recovery was put in charge of the National Radium Trust, which appointed a National Radium Commission (1932) to administer the radium. The National Radium Commission lent the radium rent-free to teaching hospitals, which were to appoint radium officers responsible for the care of the radium and for the records of patients treated. I was appointed to Sheffield, and other people appointed at about the same time were Paterson, la Touche, Thurgar, Windeyer and Wigoder. I was allowed 6 months' travel, to learn, after which I was to return to Sheffield to start work. My first concerns were with the measurement of radium using a gold-leaf electroscope, under the eye of L. A. Clarke at the Middlesex Hospital. Scattered radiation was a mystery and the amounts of radium used and its distribution in clinical work seemed purely empirical and instinctive. After 5 weeks I went to Brussels, where Murdoch and Staehl, with Mlle Simon, were using isodose distributions around radium tubes and needles to achieve arrangements giving uniform dosage in "r" units (not at that time accurately related to radium quantities) to complicated body surfaces (Murdoch et al, 1930). After 5 weeks in Brussels I went by train to Stockholm, where Heyman, Berven, Ahlbohm and Kottmeier were obtaining results based on experience with both radium and X rays. From Stockholm I wrote to Mr J. G. Graves, a Sheffield philanthropist, about the desirability of a Radium Institute and later, when the need arose, asked him to help with money for an X-ray treatment apparatus.

After a further 5 weeks I went to Hamburg, where Holthusen, Braun and Reisner were relating dose to biological effect; and then to Frankfurt, where Holfelder was using 200 kV "cannons" for X-ray treatment. After 6 weeks in Germany I returned to England, where Stanford Cade, Turner Warwick and Malcolm Donaldson, with others, were giving a course at Mount Vernon Hospital and I was able to find out the state of the art in the United Kingdom. My intention then was to go to Paris, to the Fondation Curie, but my masters in Sheffield indicated that I should return and start work.

I was shown into an empty, disused operating theatre (see Fig. 1) and, with no furniture, no staff, no radium, no beds and no experience, was given a report by Dr Rupert Hallam to read which indicated that the use of radium in the Sheffield hospitals was declining. After three days I saw my first patient in the operating theatre and turned him down: a prostatic carcinoma with a rectal fistula.

I propose to consider the development of radiotherapy since that time under two main headings: delivery and effects.

DELIVERY

The delivery of radiation in treatment can be divided into subsections concerned with (i) apparatus, (ii) techniques, (iii) dosimetry, (iv) planning and (v) execution.

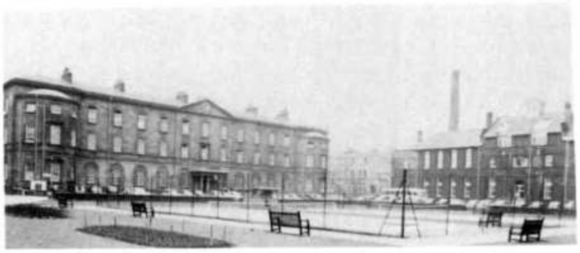

FIG. 1.

The first premises, a disused operating theatre, of the Sheffield Radium Centre (from May 1, 1931 to September 1, 1939) in the Victoria block of the Sheffield Royal Infirmary. They consisted of the upper floor under the central raised roof of the building on the right. There was a lift up to this floor. The ground and first floors were medical wards.

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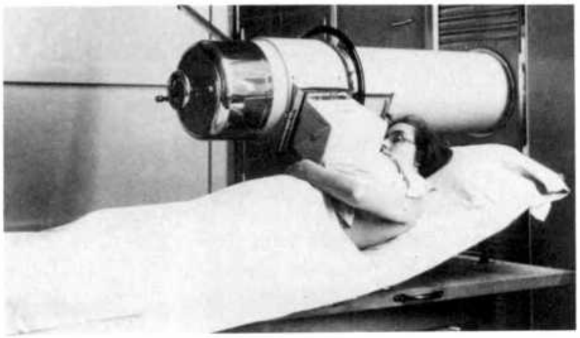

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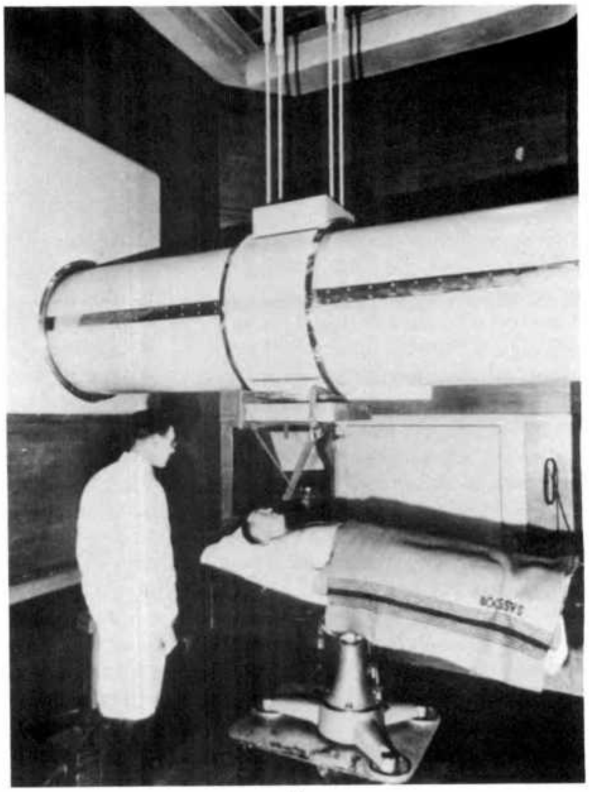

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FIG. 2.

(A) The first Metro-Vickers type of continuously evacuated steel X-ray tube, as installed in the Sheffield Radium Centre. A second tube is behind the moveable screen on the left. Behind the screen on the right are the transformer, condensers, pumps and rectifiers for a Greinacher circuit activating both tubes. It was moved on September 1, 1939 to temporary premises and later to its more permanent site after the war. Its use was terminated after about 23 years, in 1956. (B) The 1MV Metro-Vickers continuously evacuated X-ray tube at St Bartholomew's Hospital, with vertical movement of the treatment floor. (Photograph supplied by Professor Arthur Jones.)

Beam therapy apparatus

The apparatus in use has developed out of all recognition since 1930 from unprotected Coolidge tubes, the scattered radiation from which produced marrow deficiency developing some years even after treatment of thyrotoxicosis. Before the war, protected tubes with cables carrying high tension had developed, but the continuously evacuated tubes and rectifying valves installed at my request in Sheffield (Fig. 2A) were the first of a family of tubes of which the Manchester 500 kV and then the St Bartholomew's 1 MV apparatus (Fig. 2B) were natural descendants. The Sheffield apparatus, having survived two moves with dismantling and recommissioning because of the war, was only discarded in 1956. After the war the Resomax 300 kV displaced the Metro-Vickers apparatus, and then nuclear physics led to the production of cobalt-60 machines. I was allowed £1500 for the cobalt unit which we developed in Oxford with the help of H. C. Husband, a Sheffield civil engineer previously responsible for the engineering of the Jodrell Bank radiotelescope.

This one-off cobalt machine (Fig. 3) was only discarded in 1983, after about 30 years of continuous use.

Linear accelerators (linacs) were first developed in this country, as was isocentric mounting. I well remember Howard-Flanders, after explaining the principles of isocentric mounting (Howard-Flanders & Newbery, 1950), asking my opinion on the train between Waterloo and Guildford, where I went weekly to deal with my radium patients. Since then, of course, bigger and better linacs have been developed *pari passu* with betatrons delivering photon beams and electron beams up to 40 MV. I remember the thrill which I felt in 1942, when Mayneord, at a Faculty of Radiologists meeting, described the possibility of electrons, long before the machines were available (Mayneord, 1942). A 35 MV linac installed at the Churchill Hospital with the object of intraoperative electron therapy in addition to "routine" treatment had to be taken out because poor focusing of the electrons made adequate protection impossible. Further apparatus development to produce neutrons and protons from cyclotrons is now well known. The electron thrill was repeated when I read of the possibilities of negative pimesons.

D-T generators are in use for neutron treatment, but cyclotrons are in use which can produce a much higher intensity (half-value depth 8–9 cm at 16 MeV) and at higher energies (42 MeV, half-value depth 12 cm). Development of pion therapy has occurred in Los Alamos, Vancouver and Stanford University. In Switzerland it has been developed to a very sophisticated clinical level at the Swiss Institute for Nuclear Research.

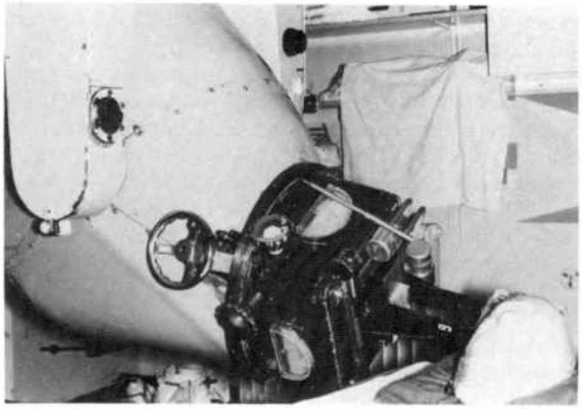


FIG. 3.

Cobalt-60 treatment head. The machine was designed to be able to fit into the angle between the lower neck and the chest with short (60 cm) FSD. The cobalt source was on a straight steel bar which retracted mechanically into the centre of a lead sphere. Collimation was by applicators fixed in one direction: 6 cm, 8 cm, 10 cm etc. up to 20 cm, but variable up to 20 cm at right angles to these. The jig was so made that only the appropriate applicator fitted. Applicators for wedged fields were black and for unwedged fields were grey.

Beam therapy techniques

The techniques used have been governed by the penetrating power and other properties of the beams available. With the contact X-ray (45–60 kV, 2–6 FSD) machines, small lesions could be treated in one or a few fractions and normal tissue effects limited to very small depths. With the 180 kV, 40 cm FSD apparatus, six or seven fields were required to treat the oesophagus. Now, with high-energy beams and 80–100 cm FSD, photon therapy of deep-seated lesions to an adequate dose is possible with three or four fields. With realistic separations the common and convenient parallel opposed pair never gives a higher dose than that at $D_{\max}$, whatever the energy, the midplane usually receiving the lowest dose. The 15–35 MV beams spare the superficial 3–6 cm. Thus, if a small tumour volume is to be boosted, more than two fields are necessary. Alternatively, combination with intracavitary or interstitial 4π (brachy)therapy, if possible, is very effective.

Wedges (Ellis et al, 1950), which I started using about 1935 (with orthovoltage X-ray equipment; Fig. 4) to modify the shape of the beam, are used now for high-energy beams routinely and are supplied commercially. Various wedge filters are regularly supplied for the beams used. With orthovoltage radiation, bolus is often necessary, so that the isodose distributions determined in a phantom are reproduced in practice as nearly as possible. With high-energy photons "compensators" were immediately found to be necessary (Ellis et al, 1959) so as to preserve skin sparing while ensuring a uniform dose to the target volume. Only with compensators can doses be "known" for a whole volume, especially when there are two contours, as in the neck. The use of a wedge as a compensator in a patient, combined with its use in beam modification as measured in a phantom, seems to me to mix two concepts. This is inherent in the computer planning of tumour treatments in which an axial plane of the beams is often the only plan. The off-axial planes near the periphery do not, except accidentally, fit the target volume (see Fig. 5).

Compensation, however, should also be attempted for tissue heterogeneities. This was attempted by Ellis et al (1964) but it was too laborious for routine treatment. However, in 1973 (Ellis & Lescrenier, 1973) I suggested obtaining two radiographs of the patient by

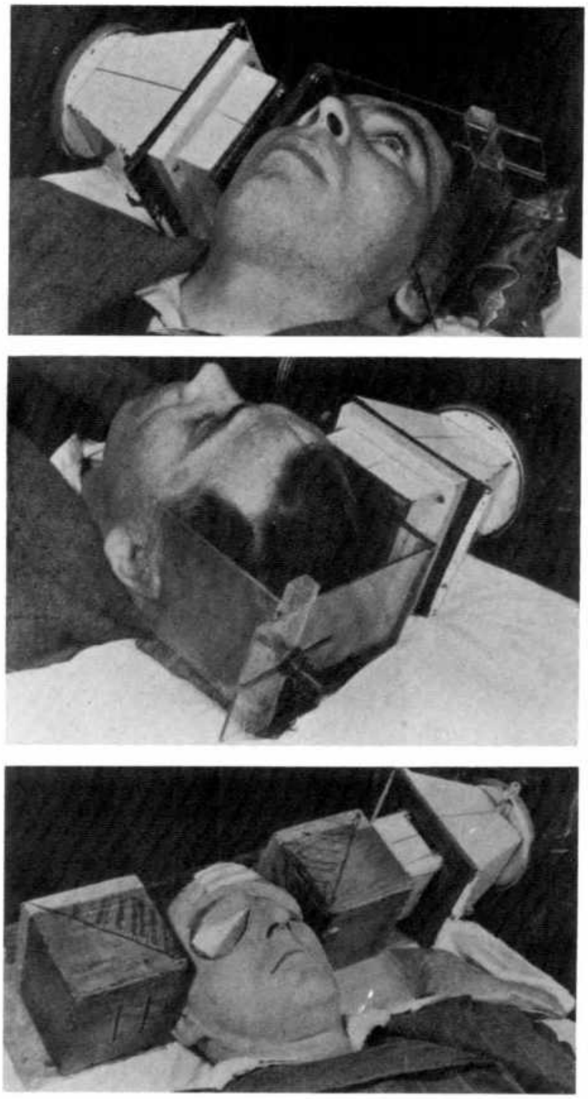


FIG. 4.

Three-field set-ups for use with wedge applicators showing (lower picture) the first primitive arrangement as used in 1935.

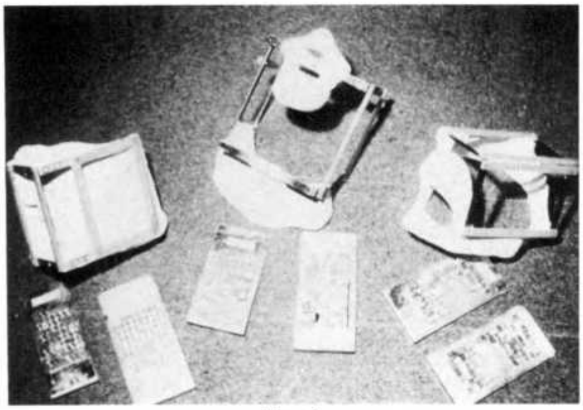


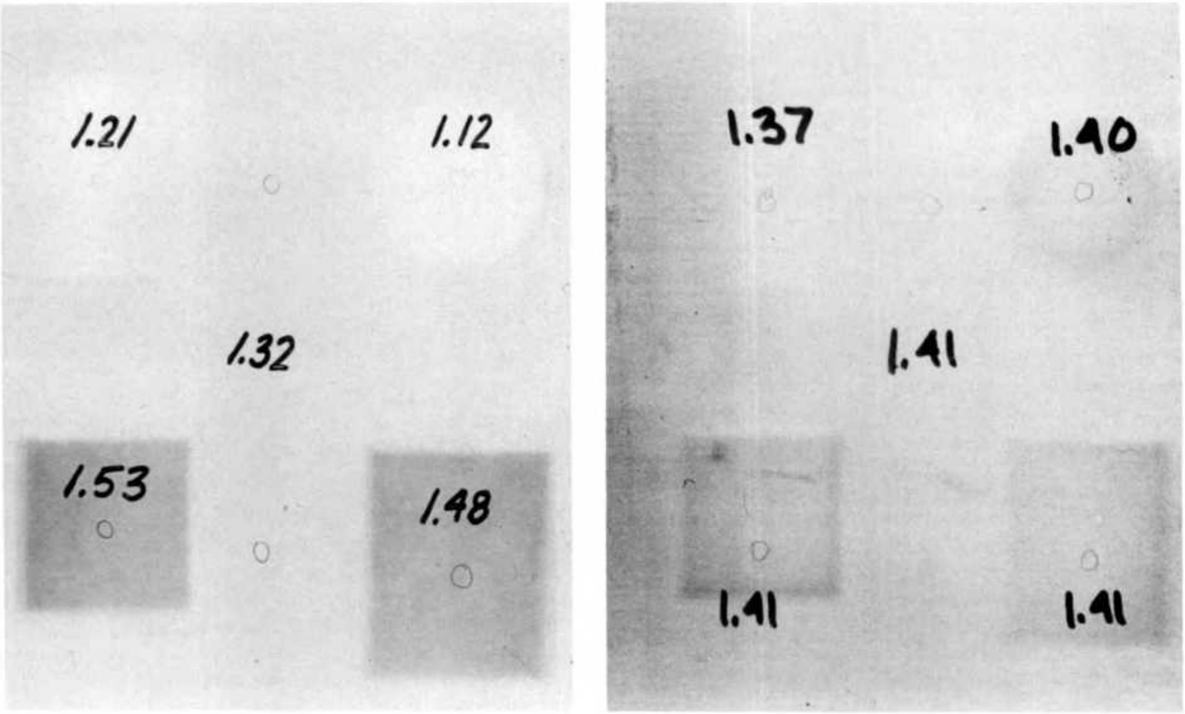
FIG. 5.

First compensator arrangements for the cobalt machine, using brass columns.

two treatment beams at right angles to provide information on the amount of matter traversed by each pencil of treatment beam. The experimental realisation was reasonable (Fig. 6).

By using a scanning densitometer calibrated for the film used, it was thought that specification of compensation for the beams used for combined contours and inhomogeneities would be possible. This method is being practised by Laursen and others (Laursen et al, 1982). Specified in this way, either the aluminium or brass column type, or the lead sheet type, of compensator could be built up for individual fields. Young and Kornelson (1983) have described compensation for heterogeneities with 10 MV X rays. With rotation therapy this is almost impossible, but for the negative pimeson facility in Switzerland, Carl von Essen has used a compensator technique, necessary for the way in which the pion beams are delivered and suitable in principle for rotation therapy (von Essen et al, 1982). In conjunction with this, the volume treated is tracked by moving the patient. This is similar to the tracking method suggested by Green and Jennings and being implemented with cobalt-60 beams (Fig. 7) by Skeggs and his colleagues (Green et al, 1960; Davy et al, 1975). The original intention to track along the lymphatics of the pelvis, abdomen and thorax with a sharp gradient outside the target volume (so as to spare bowel, kidneys, spinal cord etc.) is best fulfilled with a small-penumbra beam.

The ultimate in this type of method for localising the beam to the target volume is by scanning the whole field



A

B

FIG. 6.

Experiment to demonstrate the possibility of total compensation (for both contour and heterogeneity) using various densities. (A) Without compensation shows ±16% variation from unit density; (B) with compensation arranged according to X-ray film (immune to wavelength variations) shows a maximum variation of only 2.8%.

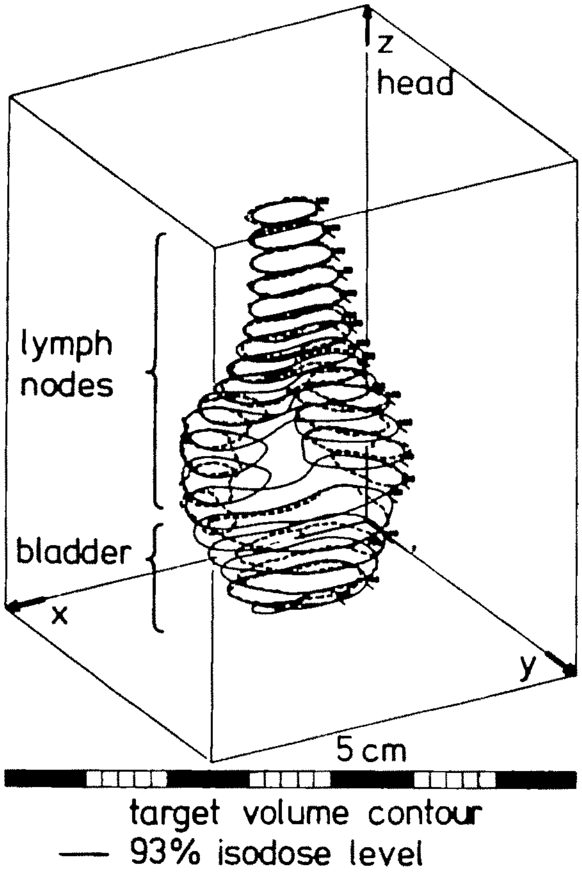


FIG 7.

Diagram showing the isodoses obtained by tracking, as used with the cobalt machine at the Royal Free Hospital A similar distribution diagram has been published by the Swiss Institute for Nuclear Research using pions.

with a continuously variable beam. Goiten and Chen (1983) have described a method to do this with protons, both with and without an external compensator, depending on whether a thin pencil or a 2 cm beam is used. With protons, as with pions and heavy ions, the Bragg peak geometry of the isodoses makes such a method more possible than it is with photons (Suit et al, 1982). With electrons, however, it should be possible in principle to use suitable compensators to cover a field so that the penetration and build-up of the beams are controlled and the dose to the tumour and the normal tissues can be known.

One of the growing points in connection with apparatus and techniques is cost. From the time when the most modern apparatus, two X-ray tubes with transformer, condenser and rectifiers, cost £1500 and the treatment couches were light wooden structures with instantaneous braking (Ellis et al, 1955), is a far cry to the present day, when the cheapest machine cost is of the order of £250 000 and the cost of the treatment couch is about £5000. It is a further cry still to pions and further yet to heavy ions.

The fundamental research from which was developed all of the above expertise as well as that in the use of radionuclides has been carried out by physicists, from whose results, coordinated both by manufacturers and by academic bodies, insight has been gained into the properties and interaction with matter of the radiations, enabling the development of the necessary machines for their administration. Moreover, the commissioning and maintenance necessitate continual physics help.

Radionuclides

Radiation therapy has derived much impetus from the availability of radionuclides. In the 1940s thorium X provided a means of alpha particle radiation which was used to destroy residual cells and small projecting lesions in the bladder In the 1930s beta particles were used from applicators using radium covered with Shellac. Glass radon seeds were succeeded by needles and tubes screened by gold or platinum, so that gamma radiation became the logical and common source for intracavitary and interstitial treatments. Uneven loading of all these resulted in uncertainties, which were compounded if there were leaks of radon from radium needles. There was a period in which cobalt-60 wire and powder were used and phosphorus-32 solutions used on blotting paper and in forms such as "plasma pudding".

In addition, solutions containing gold-198 and yttrium-90 colloids developed for local applications and phosphorus 32 and iodine 131 systemically. The therapy rationale of these uses was sound; the safety was questionable. The long half-life hazards of cobalt 60 and radium have determined their discontinuance. Now the use of indium 192 and of iodine 125 for interstitial, and of caesium-137 tubes and needles for intracavitary and interstitial treatments have become standard practice, especially allied to Henschke's afterloading principle (Henschke et al, 1963). In several situations the electron beam may be substituted for interstitial and surface applications.

Dosimetry

It is axiomatic that unless the dose is known, correlation of dose and effect is impossible. The role of the physicist in making it possible to do this is absolutely vital. In the 1930s, Sabouraud pastilles and erythema doses were still being used as units. However, agreement having been reached at the Second International Congress of Radiology in Stockholm, the rőntgen unit depending on ionisation was formally adopted. In radium work the principles of distribution of sources was one of my chief concerns, but the value of 8.3 R at 1 cm from a 1 mg radium source screened by 0.5 mm platinum was settled for me when I heard Mayneord in 1933 describe its determination by him and Roberts at the Annual Congress of the British Institute of Radiology (Mayneord & Roberts, 1934). Before this, estimates with the "absolute" chamber by the National Laboratories of USA, France, Germany and the UK (4–7 rad/mg/cm) had been very confusing. The absolute chamber was designed to measure all the ions produced in 1 cm^3 of air corrected for NTP in accordance with the definition of the röntgen. In 1956 the ICRU distinguished between exposure to radiation and absorption of energy by using the röntgen for the former and the rad for the latter. Though they were almost numerically equal for soft tissues, they differed considerably for bone, especially for "soft" radiation (HVL 1–4 mm Al). From a practical point of view, a direct use of the numerical values when calibration is in rads from experience gained with calibration in röntgens resulted in overdosage. The necessary physical factors and fundamental concepts have all been gradually stabilised, from Gray's quantitative development of Bragg's cavity theory up to Burlin's general theory of cavity ionisation.

Perhaps this aspect is not growing further, but detailed measurements and calibrations are still proceeding. The system of primary and secondary calibrations and of international comparisons using not only ionisation but calorimetric, chemical and thermoluminescent dosimetry have all tended towards less variation between centres in their published doses.

My original dosimetric arrangements were crude, but relatively satisfactory. Using a Hammer dosemeter with a chamber of > 1 cm internal diameter, I had a dustbin modified to act as a water phantom, ensuring that the distance from its wall to the ionisation chamber was greater than the range of the secondary electrons (10 cm) for all measurements. The measurements involved moving the whole dustbin on rails (two sets at right angles) so that the cross-field isodoses as well as depth doses were measured by myself and G. S. Innes, who was the engineer sent by Metro-Vickers to see my continuously evacuated apparatus through its teething troubles. Now measured doses with photons can be expected to be uniform to ±5%, provided errors in centring and collimation are avoided and calibrations carried out daily. Build-up and build-down phenomena, however, in cavities of the dimensions of the larynx and bronchi and the mouth can result in *unavoidable* reduction of dose at surfaces inaccessible to bolus, where, unfortunately, ulceration implies the highest proportion of hypoxic cells in a tumour. For research purposes, for instance with protons, neutrons and pions, dosage determinations are usually carried out with a maximum of expertise and numerous checks. Protocols for optimum accuracy of dose estimation for photons and electrons by working parties in the USA and UK (American Association of Physicists in Medicine (AAPM), 1983; Hospital Physicists' Association (HPA), 1983, 1985) indicate the vigorous growth of the dosimetric side of radiation therapy. The complexity of giving a dose to a patient in accordance with a planned prescription is such that radiotherapists cannot work without the backup of physicists and technicians.

Dosage with 4π therapy depends very much on the dosage distribution relative to the tissues *and the* tumour. Without a prepared template, doses tend to vary from what is intended. The first radium implants I saw in 1930 involved insertions of a large number of needles into a cancer of the maxillary antrum. The prescribed amount of radium was "lots"! The dose was in milligramme hours. In Brussels, Murdoch et al (1939) were using a mainly peripheral distribution to achieve a uniform dose in "röntgens", but the *k* factor was uncertain. In Sheffield needles were requisitioned by surgeons for 1 week and were inserted with no prearranged plan or fixing stitches, so that they fell out randomly during "their week". To try to remedy this state of affairs, I made wax models of tumours and their surroundings with pins with coloured heads to indicate the type and position of needles to be used. I was soon asked if I would like to do an insertion and within weeks was doing them all, with 20 beds at the Royal Infirmary and six at the Royal Hospital, and any necessary at the Jessop Hospital for Women.

The dosage for cervix carcinoma followed the Stockholm timing because interstitial insertions at Radiumhemmet used needles containing about five times the linear intensity of radium, which were left for 24–48 h; and, because 1 week had been used previously, I inserted the Sheffield needles 1 cm apart and left them for 1 week. I was trying to evolve by experiment a system of dosage when I was told by Ralston Paterson of their physicist, W. M. Parker, who had worked out a system of radium dosage (Paterson & Parker, 1934) and I spent a summer holiday near Manchester with my wife and firstborn in 1933 to learn the basis and the practice of the Paterson–Parker system before it was published, and how to modify it when all the needles were of the same linear intensity. Since then, to this day, I have found the Paterson–Parker system generally satisfactory, with modifications introduced to fit advancing ideas about suitable radionuclides, about the nature of tumours and about what are suitable spacings and distribution of the needles.

In particular, in 1931 I prepared a wax collar with one line (of radium tubes) expanded at the end to treat massive glands in the neck at an almost uniform distance of 7 cm so as to get as good a depth-dose as possible. The glands disappeared, but the patient died of marrow insufficiency. I realised then that the bone marrow had also been heavily irradiated, and therefore asked the Sheffield Radium Centre Committee for apparatus for beam irradiation. Experience at other hospitals made them refuse a radium beam unit, and so I started to try to get an X-ray machine. Glasser et al (1968) published a system suited to the implantation of a tumour with small seeds and, since the development of iridium-192 wire, Pierquin et al (1978) have published a system which is more related to the tumour than to the radiation field. The most recent system, which can be applied to very large areas and is, thus, suitable for the rapid estimation of doses for implants which cover the operation field at the time of surgical excision is the nomogram made for use at the Memorial Hospital, New York (Anderson, 1982).

Planning the treatment of a patient involves decisions about the method of management, which is increasingly multidisciplinary. If a patient has cancer the radiotherapist should be involved *before anything is done which may prejudice the issue*. The actual planning of the treatment by radiation has developed apace, from the use of a piece of cardboard (which was cut to the contour of the patient and had marked on it the position, direction and diameter of the fields being used) through the use of the pin and arc and the back pointer, first mechanical and now optical, with precision methods to ensure that the beam of radiation does what is planned. Body sections, as in the atlas by Eycleshymer and Schoemaker (1911), have been invaluable and can still be useful, although the simulator and, later, computed tomography (CT) radiographs have added to the precision of knowing where the tumour is About 1933, at a visiting club meeting, the question was hotly debated between Fulton and Stebbing as to whether artificial aids such as radiographs were more accurate than clinical determination to decide where to treat. Now, although CT is not always necessary, this, ultrasound and soon the added refinements of nuclear magnetic resonance (NMR) may be called upon to decide the position of a tumour and, by tattooing sufficient points, to ensure that the position and direction of a beam can be recalled at any time. Such recall could be useful as a research project to determine the amount of contraction occurring in skin. The precision and facility with which technicians position patients with the electrical aids available today is impressive. I remember, however, being unfavourably impressed in 1937 by a treatment, positioned by a radiologist using the latest 1000 kV machine, to a pelvis through the patient's trousers with his keys still in his pocket! The precision which can now be achieved in treating a baby's eye, shielding the lens, with 6 MV X rays, and in treating a prostate gland with protons or X rays should inspire all radiotherapists

Tracking technique. The development of "tracking", following the concept of T. A. Green (Green et al, 1960) and now called "conformation therapy" (Davy et al, 1975) has become more practical with the development of computers. At Villigen in Switzerland, in the pion facility, this principle is used in clinical treatment.

The extent of the tumour and target volumes. Even now, especially when it is difficult, the radiotherapist may fail to define the tumour volume clearly and, dismally, to define the subclinical volume. This is not surprising, because subclinical extension has not been sufficiently investigated. In the skin it should be relatively easy to determine, but is usually only guessed. Knowledge of subclinical extent in the lung could be very important in reducing complications, while improving the effect on the primary tumour. Perhaps this could be an important and rewarding area of determining new knowledge. Computer planning has come to stay, but the radiotherapist must still define the volume to be treated and this should be in three dimensions. The important growing point is not only interfacing of computer planning with CT but also designing and making compensation for contours and tissue heterogeneity. Every issue of medical physics and radiology journals shows that this branch of medical science is still a vigorous plant which will continue to solve problems of giving known doses of radiation to wherever necessary.

EFFECTS

It is not enough, however, to deliver the doses; it is important to know and control the effects of the radiation so as to kill the tumour while preserving normal tissues. A quantitative appreciation of the effects of radiation on tissues and organs is desirable, if not essential. Because the tissues are alive, the time factor and number of fractions, as well as the dose, are important. The former modify the effect of the latter. In the 1930s Wintz (1932) gave large single doses of irradiation to the pelvis (1500 r). Heyman (1925, 1927) and Forssell (1928) decided, by observation, on an optimum timing for radium treatment of carcinoma of the cervix uteri. Regaud and Ferroux (1929) showed that a fractionated treatment sterilised the rabbit testis more effectively than a single dose large enough to cause skin necrosis. At weekends and holidays I tried to find the effect of radiation on a nerve impulse, whether pressure modified the skin reaction, if there was a loss of vessel tone just before a skin reaction, and whether irradiation through the heart affected the ECG during radiation or afterwards, immediately or long term. I also formed a hypothesis that radiation had its effect on living matter by breaking molecules by displacing electrons, and thus breaking valency bonds which were sometimes prevented from rejoining because of Brownian movement. I also had an idea that tumour cells attracted a blood supply, because the products of metabolism of the cells stimulated division of endothelium.

Clinically, I found that 4000 r in 24 h with radium produced a similar effect on skin to 7000 r in 8 days and that, using 180 kV, if I treated patients three times weekly (so as to be able to cope with more patients than if I were treating them six times weekly), the dose that was given in the same overall time treating three times weekly in 1 month should be reduced, judging from the skin reactions, from 5000 to 4500, *i.e.* by at least 10%.

For what it was worth, I saw no other difference in skin, mucous membrane or tumour effect, but this was in 1934. It took me 25 years to realise the significance of this difference, when I started to worry about separating the time, dose and fractionation effects on a quantitative basis Cell survival data seemed promising, but provided no time factor. In 1965 I worried something out which, from calculations on hundreds of Oxford patients taken, in my judgement, to normal tissue (skin

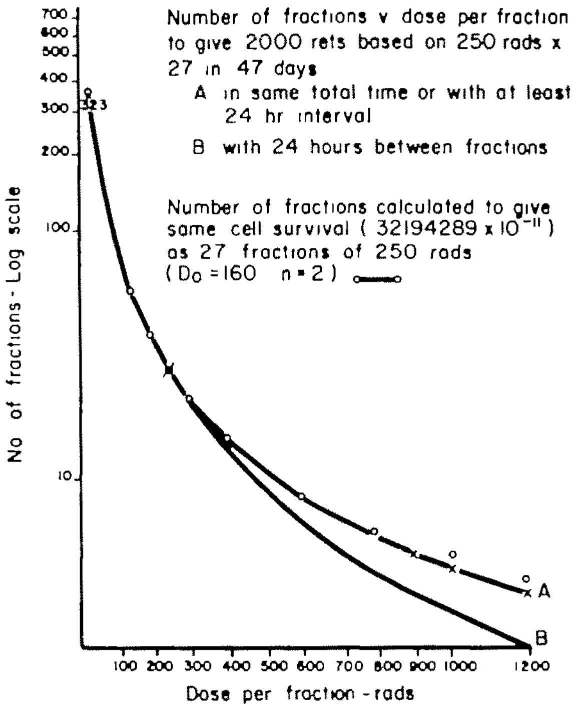


FIG. 8.

The close relationship between the NSD (— × — ×) and the cell survival (– ○ – ○ –) using $S_N = [1-(1-e^{-d/d_0})^n]^N$ The correspondence is almost exact with $n = 2\ 2$ and $d_0 = 150$ (calculation 1970)

or mucous membrane) tolerance, seemed to fit well the formula $D = Nd = \text{ESD}.N^{24}T^{11}$ where D = total dose, d = unit dose, N = no. of fractions, T = overall time. NSD was substituted later for ESD by a panel in Geneva of the World Health Organization. In view of the differences between centres of accuracy of dosage and of judgement of clinical tolerances by different therapists, I considered that each should determine his/her own NSD at that time. The NSD formula was developed in response to the need to separate time and fractionation in their effects on normal connective tissue, and I propose to list some aspects and uses of it which are helpful in radiotherapy.

The TDF

The principle of partial or, as I prefer, proportional tolerance is implied in the first publication (Ellis, 1967). As calculated from the NSD formula, 31 treatments of 200 rad given five times weekly in an overall time of 6 weeks give an NSD of 1800 rets.

$$\text{NSD for } 16 + \text{NSD for } 15 \text{ fractions}$$
$$= 1169 + 1120 = 2289 \text{ rets}$$
$$\text{but } \frac{16}{31} + \frac{15}{31} = \frac{31}{31}$$

i.e. the proportions of the 1800-ret tolerance schedule should be added together. This was emphasised later by Winston et al (1969), and put in the form of time, dose and fractionation (TDF) factors by Orton and Ellis (1973). I then realised that if the number of fractions for 1800 rets (≏ 100 TDF) is N, then the TDF for a fraction of the same size delivered with the same frequency (*e.g.* 5/week, 2/week, 2/day) is 100 n/N, because 1800 rets is a TDF of 100. Since N can always be found from the NSD formula, the TDF can be determined from the NSD formula for any type of schedule or partial schedule. TDFs, being based on proportional tolerances, can of course be added, so that summated biological effects can be obtained. Similarly, for low-dose-rate continuous radiation, if, with a certain dose rate, r rad/h, 1800 rets is given in time T hours ($T = 2.1 \times 10^4 \times r^{-1\ 35}$) then, since 1800 rets ≙ 100 TDF, with the same dose rate in time t h, the TDF is 100 t/T (Orton, 1974).

NSD and cell survival can be correlated, as shown in Fig 8, in which number of fractions and rads/fraction are plotted for the same NSD in the *same total time*. Svoboda (1978) has published data relating degree of reaction to schedules of radiation. Withers and Peters (1980a) have specified cell survival parameters for normal tissues. The NSD/TDF relationship is compared with calculated cell survivals in Table I. It seems that the clinical reactions correspond better with the TDF than the cell survivals calculated with these parameters.

Fraction size and cell-killing

However, in attempting to decide on cell survival principles and the merits of different fractionation schedules in eradicating tumours, it seems that with high extrapolation numbers a small number of large fractions for the same NSD would have a greater cell-killing effect. This has proved to be the case for melanoma and for other difficult tumours (Ellis & Goldson, 1977).

Malignant melanoma and large fractions

It is useful at this point to explain why I consider that most of these tumours may be successfully irradiated but not always with ordinary fractionation schedules. My thesis, written in 1937 for the FBAR (subsequently FFR and then FRCR) on the radiosensitivity of malignant melanoma (Ellis, 1939), was based on interstitial treatment of metastases or recurrences after surgery. Long-term survival was, therefore, impossible but the eradication of many treated lesions certain. I have realised since that my experience with beam therapy had been based on large single doses to small lesions, usually on the face or neck, using contact X rays (1800 rad minimum tumour dose) and a few large fractions for widespread hopeless lesions, referred when all other methods have failed. The small lesions were usually eradicated. The widespread lesions invariably responded. *All* were proved by biopsy immediately after the treatment. Thus, I plead for trials of treatment of early lesions by continuous low-dose-

TABLE I

CLINICAL NSD–TDF VS CELL SURVIVALS: EQUATION USED $S = \exp(-(2.86d10^{-3} + 3.2d^2 10^{-6}))$

Reaction score	Schedule (rad)	Time (days)	NSD	TDF	Cell survival
3	15 × 300	5	1910	111	0.34×10^{-7}
	15 × 300	9	1840	104	0.34×10^{-7}
	25 × 260	35	2030	121	0.37×10^{-10}
2	20 × 225	5	1800	100	0.101×10^{-6}
	20 × 237.5	5	1900	109	0.34×10^{-7}
	24 × 200	10	1725	94	0.51×10^{-7}
	15 × 300	21	1700	92	0.34×10^{-7}
	24 × 184	10	1590	84	0.24×10^{-6}
	15 × 250	5	1620	85	0.11×10^{-5}
	24 × 210	10	1840	104	0.19×10^{-7}
	30 × 158.3	12	1850	105	0.12×10^{-6}
	30 × 183	42	1610	84	0.61×10^{-8}
	25 × 260	70	1875	107	0.37×10^{-10}
1	20 × 213	5	1710	93	0.28×10^{-6}
	30 × 150	12	1510	77	0.30×10^{-6}
	32 × 148	12	1570	80	0.14×10^{-6}
	25 × 220	70	1600	76	0.31×10^{-8}
	50 × 120	35	1580	81	0.35×10^{-8}
0	15 × 267	5	1700	91	0.34×10^{-6}
	32 × 141	10	1530	78	0.32×10^{-6}
	50 × 120	70	1475	71	0.35×10^{-8}
	50 × 130	70	1590	81	0.57×10^{-9}

3 = Skin leathering and muscle fibrosis or bone necrosis, skin or pleural scarring; 2 = moderate skin thickening and muscle fibrosis, 1 = mild skin thickening; 0 = normal. Analysis of results reported by Svoboda (1978).

There is greater spread of cell survivals in any group which represents a clinical result than of NSD–TDF values.

rate treatment, large single doses or a few large fractions. My figures given at the Montreal International Congress of Radiology in 1962 were, heartbreakingly, lost in Canada. The overall survival was of the order of 30% at 5 years.

Late effects of large fractions

As shown by Turesson and Notter (1979), the late clinical effects of radiation relative to CRE or TDF are greater with large single fractions or higher dose rates for the same NSD. Turesson and Notter suggest correction factors according to fraction dose and size, the use of which in the NSD formula corresponds to the same late clinical effect on skin.

> *e.g.* 615 rad/fraction, 7 fractions, 1 F/week give 1800 rets = 100 TDF and the same acute clinical reaction as 31 × 200 rad at 5 F/week.
>
> However, for the same *late* effect as 31 × 200, the correction factor 1.08 should be used in the formula giving 615 × 1.08 = 664 rad.
>
> 7 fractions of 664, 1 F/week would have the same early effect as 35 × 200 at 5 F/week (1920 rets) while, for the same late effect as 31 × 200 (= 100 TDF), the TDF would have to be (6.45/7) × 100 = 92 TDF. For organs other than connective tissue the same factors may not be valid. The most important are spinal cord, kidney and lung.

Withers and Peters (1980b, Fig. 2.29) compare 460 (2 F/week) × 13 with 200 (5 F/week). The latter 32 × 200 (5 F/week) gives 103 TDF for both early and late effects. 13 × 460 (2 F/week) gives 129 TDF (early effect) and 139 TDF (late effect). Their suggested 13 × 360 (2 F/week) gives 88 TDF (early effect) and 93 TDF (late effect). For 103 TDF (early effect) 13 × 398 (2 F/week) and for 103 TDF (late effect) 13 × 385 are needed (all doses in rads). Their comparison of 3 × 460 2 F/week with 32 × 200 5 F/week seems to be quite unjustifiable.

Low-dose-rate radiation

Most radiotherapists with experience of low-dose-rate radiation favour its use. Applied rationally, the results are rewarding in many cancers such as cervix, tongue and oropharynx either alone or, preferably, as a local "boost" combined with about 60 TDF external radiation. Dose-rate modification of effects relative to dose have been used clinically for several years. Doubts about its validity have been freely expressed. It might be that clinical conditions are too coarse to make its use worthwhile. From a radiobiological point of view I cite three supporting facts.

(1) The isoeffect curve used clinically for many years was fitted, when cell survival data became available, by points calculated by Ray Oliver on the basis of $d_0 = 160$, $n = 2$ and a half-life of 30 min for sublethal damage (Fig. 9A).

(2) The work by Mitchell plotted in Fig. 5 by Orton (1974) fits a line with the same slope as one based on the above and on Paterson's dose-rate relationships (Fig. 9B).

(3) From cell survival data related to dose-rate, Withers and Peters (1980b) ignore the slope in the low dose-rate region which does, however, suggest the qualitative validity of such a correction (Fig. 9C).

The equation (T for 100 TDF $= 2.1 \times 10^4 \times r^{-1.35}$) derived by Orton is related to the time for 1800 rets and thus for 100 TDF. Times with the same dose-rate give TDFs proportionally. For instance, if the time for 1800 rets is 120 h, 80 h at the same dose rate would give (80/120) × 100 TDF.

Organ sensitivity

The fact that some organs and tissues are more prone to complications with doses of radiation tolerated in other tissues has been known for some time, although the basic tissues in any organ responsible for healing are the capillary endothelial cells and the fibroblasts. Certain individual organs are essential to life, however, and they must be so considered. It has been possible to derive formulae of the type $Nd = \text{NSD}_{\text{organ}} N^x T^y$ for

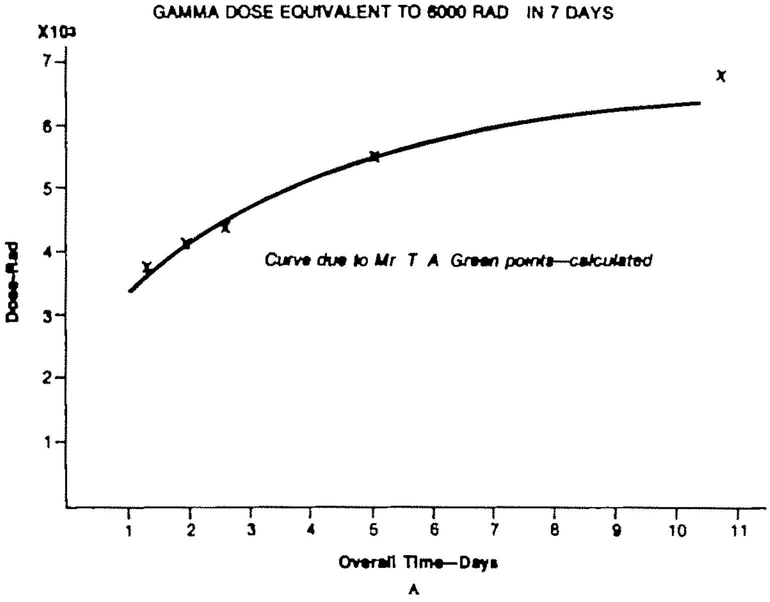
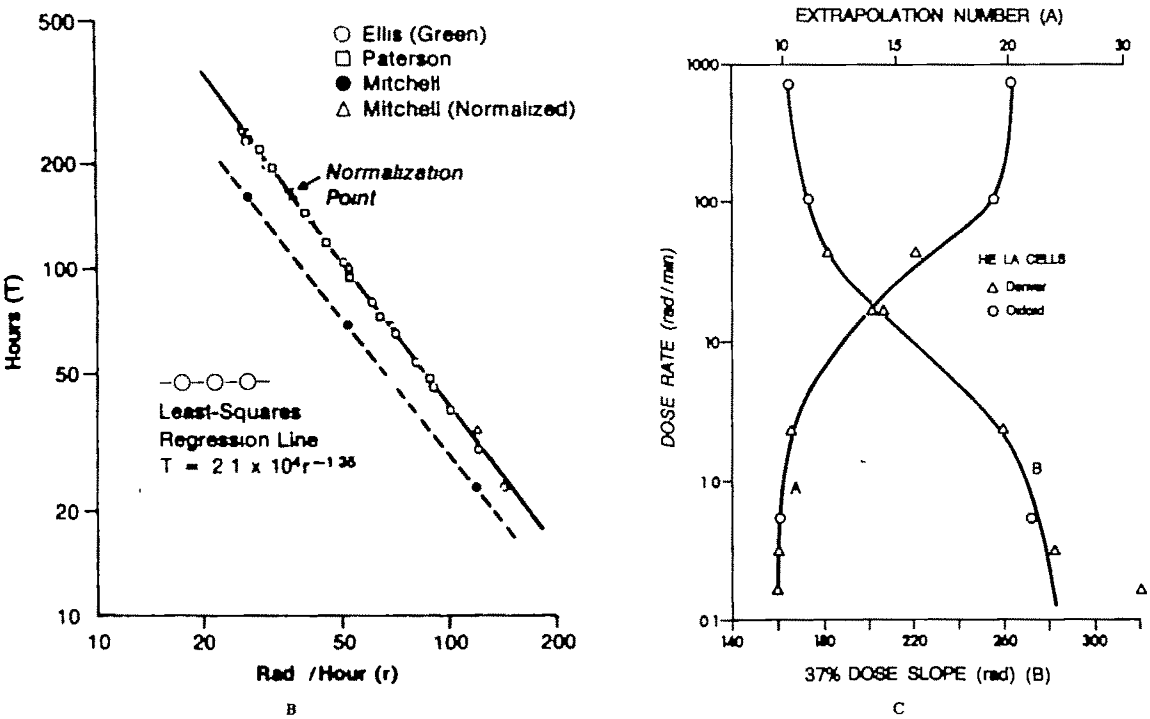


Fig 9

(A) Isoeffect graph derived clinically and in clinical use for many years before Puck and Marcus. The crosses were calculated by R. Oliver, based on $D_0 = 160$ and $N = 2$ for equal effects based on a half-life of 30 minutes for healing of sublethal damage of cells. (B) Treatment times at different dose rates that result in biological effects equivalent to those produced in 168 h at 35.7 rad/h. (The original data reported by Mitchell represented the equivalent to about 113 h at 35.7 rad/h (— — ● — —) and each point has been normalised by increasing the time by a factor (168/113). The times correspond to 1800 ret (~ 100 TDF). Reprinted from Orton, 1974. (c) Curve B shows definite change in d_0 between 120 and 10 rad/h (2–0.2 rad/min) (From Withers and Peters, 1980a, data from Hall, 1972.)



several organs (see Table II). Some say that such formulae are unnecessary, since 200 or 180 rad fractions should be used, but when an organ is irradiated incidentally the doses are not always the same and it is desirable to estimate the relation of the dose to its tolerance level so as to avoid injuries due to radiation such as myelitis, nephritis or crippling pneumonitis. In this connection I have felt guilty, during the last few years, that a patient I treated for carcinoma of the oesophagus in 1934 was not reported. He was treated through six fields, and developed weakness in his legs 4 months later. Because at that time the central nervous system was insensitive to radiation—everybody said so—I thought he must have a metastasis in the cord, which I dared not treat through his already telangiectatic skin. When, after 3 months, he began to recover I decided that he had received a bare tolerance dose of radiation to the cord, namely 4150 r at 180 kV (= 4600 rad Co). Since then I have tried not to exceed this dose to the cord. If I had reported this perhaps many patients would have been saved serious trouble. My excuse is that I was single-handed and had no time for or experience in publishing anything. My practice since then has been to limit cord doses to this level but, even so, I made a mistake in one case of massive carcinomatous neck glands and caused a radiation myelitis.

The above formulae, like the original NSD equation, should be considered as methods of charting a radiotherapeutic course through an uncertain sea with a view to making changes according to experience. Progress in radiobiology has been such that it has been possible to develop an α/β ratio for different organs which is based on the effect of single and multiple chromosome breaks as represented by the linear-quadratic expression for cell survival. The survival equation is

$$S = [\exp(-(\alpha d + \beta d^2))]^N$$

where d is in gray and N is the number of fractions.

Table II shows various values of α/β Clearly, these are organ-dependent and this system should eventually replace the empirical NSD–TDF system. One difficulty about it, however, is that it takes no account of time. While time might possibly not be important for late effects, there is no doubt that it is important for early effects on connective tissue—see Fig 10. Another difficulty is that the system may not apply to organs as it does to cells. Moreover, at present there seem to be no values of α/β available to fit brachytherapy patterns. Suit (1983), in his Failla Memorial Lecture, has reviewed the impact of radiation biology on radiation therapy in masterly fashion.

Uterine high-dose-rate treatments

Changes to high-dose-rate fractions for intracavitary radiation for endometrial and cervical cancer can be adjusted on the basis of the NSD–TDF system. Joslin et al (1972) were the first to develop high-dose-rate protocols. Merkas and Vujnic (1976) made the adjustments according to the TDFs and the results so far indicate that, in complications or cancer control, there is no significant difference from their low-dose-rate experience.

TABLE II

ORGAN SENSITIVITIES

Reference	Nd = NSD. $N^x T^y$ d and NSD in rad and ret	α/β ratios (Gy) (26 days) $N = 20$ or $d = 200$	Fowler (1983)
Connective tissue			
Ellis	$1800\ N^{24}T^{11}$	4.8	9–12 (E)
Brain			
Cohen (1983)	$769\ N^{56}T^{03}$	0.66	
Spinal cord			
Wigg et al (1981)	$860\ N^{46}T^{09}$	3.4	
Wara et al (1975)	$1197\ N^{377}T^{058}$	1 5	1 0–4 9 (L)
Sheline (1980)	$1016\ N^{44}T^{05}$	0 44	
van der Kogel (1977)	$1251\ N^{37}T^{05}$	1 47	
Cohen (1983)	$1017\ N^{42}T^{06}$	0 86	
Kidney			
Hopewell & Robins (1983) (F.E)	$500_{k1}N^{49}T^{11}$	0 095	1.5–2 4 (L)
Kunkler (1952) (F.E)	$390_{k2}N^{49}T^{11}$	0 078	
Cohen (1983)	$465\ N^{25}T^{19}$	2.7	
Lung			
Rubin & Casarett (1971) 5% pneumonitis	$800\ N^{36}T^{1}$	1.37	2.4–6 3 (L)
no pneumonitis	$660\ N^{36}T^{1}$		
Phillips & Margolis (1972)	$687\ N^{38}T^{1}$	1 1	
Ellis	$660\ N^{3}T^{1}$	2 06	
Cohen (1983)	$1116\ N^{25}T^{04}$	3.5	
Lens			
Merriam & Focht (1957) (F E)	$220\ T^{175}$	2.6	
	$220\ N^{15}T^{025}$		
Gut			
Cohen (1983)	$15.82\ N^{29}T^{08}$	1.53	6–11 (E)

E = early effect, L = late effect, F.E. = calculation by present author

To determine α/β according to Fowler (1983): $\dfrac{N_1 d_1}{N_2 d_2} = \dfrac{\alpha/\beta + d_2}{\alpha/\beta + d_1}$

If NSD isoeffect formulae are used with "clinically satisfactory" data for two schedules, α/β can be determined, *e.g.* for gut, (Cohen) using 27 8 × 2.00 and 20 × 2.46, α/β = 1.53 Gy for a late effect.

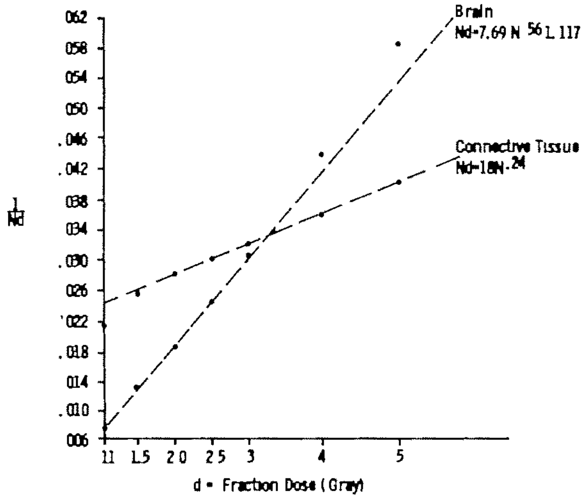


FIG. 10.

Linear quadratic graphs plotted for tolerance levels using the formulae shown and based on $d = 2$ Gy and 2.5 Gy. The connective-tissue graph is drawn with Turesson and Notter corrections Uncorrected, the points for 3, 4 and 5 Gy would fall below the graph at $1/Nd$ values of 0.032, 0 035 and 0.038, respectively, instead of the values 0.032, 0.036 and 0.040. The brain graph drawn from Cohen's formula for 2 Gy and 2 5 Gy passes through points for $1/Nd$ corresponding to 3, 4 and 5 Gy of 0.0305, 0.041 and 0.0535 whereas the points calculated from the formula are 0.0305, 0.044 and 0.0585, equivalent to corrections for these of 1.00, 0.97 and 0.96, respectively—a smaller effect of large doses than represented by the formula. Other clinically derived formulae can be examined similarly

Area and volume corrections for the NSD are used by some but, because the essential effect of radiation is cell-killing, I think that no such correction should be applied. Moreover, the basis of this correction is work on skin reactions carried out before the importance of dose–cell survival parameters was realised. The area of killed epithelial cells, especially with flat-ended applicators, was larger with the larger doses in the middle of large fields. The recent work by Hopewell and Young (1982) shows that with a uniform dose to an area there is no area correction required. The volume corrections are derived from area corrections and so there should be no volume correction necessary. I disclaimed the necessity for this before 1972

Instead, the important principle should be the proportion of an organ irradiated to a high dose. Thus, the length of bowel, the proportion of a kidney, the length of spinal cord and the proportion of the perichondrium of a cartilage—especially such a small cartilage as the arytenoid—seem to be much more realistic bases for dose adjustment than volume *per se* For instance, to ensure that only part, instead of the whole, of the arytenoid cartilage is enclosed in the high-dose volume in treating a laryngeal cancer considerably reduces the risk of necrosis (Wang, 1983).

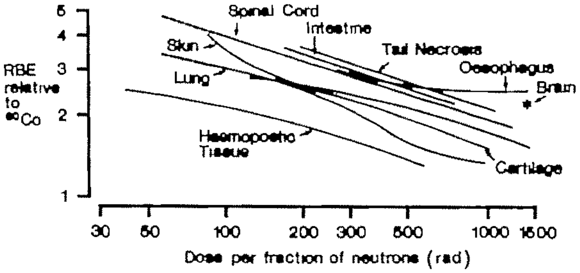


FIG. 11.

RBE (relative to ^{60}Co) vs dose per fraction for 16 MeV (d,Be) neutrons· the RBE for ^{60}Co was taken as 0 9. Ed = 16 MeV (Be) (From Field & Hornsey, 1979.)

NSD, TDF and the RBE

The RBE was first defined with reference to 200 kV radiation. High-energy radiation has less biological effect per rad than orthovoltage. The ratio is difficult to establish. I found clinically, for oral mucous membrane, that an RBE for ^{60}Co γ rays of 0 9 was more satisfactory than 0.85, so that for 1800 ret (= 100 TDF)

$$Nd_{\mathrm{Co}} = 1800\ N^{.24}T^{.11} = Nd_{\mathrm{kV}}/0.9$$

For fast neutrons it has been shown that the RBE varies with the size of the fraction dose (Fowler & Morgan, 1963; Catterall & Bewley, 1979). This is exemplified by the graphs shown in Fig. 11. If a uniform RBE is used it seems that the biological effect is underestimated for small dose fractions. This implies that a constant index for N may not be justifiable. Field and Hornsey (1979) suggested that $N^{.04}$ should be used for fast neutrons, but perhaps the equation should be $Nd\,\mathrm{RBE}_{N_e} = 1800\ N^{.24}\ T^{.11}$ when RBE is adjusted to the d_{Ne}/fraction. If this is done in terms of proportional tolerance (= TDF), a comparison between the isoeffect curves in reproducing a tolerable cobalt treatment to the pelvis, and those using a uniform RBE of 3, can be made (Ellis & Weatherburn, 1984). If, for photons, the bowel tolerance in pelvic treatments is considered to be the equivalent of 25 × 200 rad (= 25/31 = 0.81 ≃ 81 TDF), it is seen that all the bowel in the pelvis can receive more than a tolerance dose (Fig. 12), providing a possible explanation for the severe complications reported by Arnot (1982) from the Edinburgh neutron facility.

von Essen et al (1982), using negative pimesons, have derived the equation $D = kT^{0.11} N^{0.10}$. Variation of RBE with fraction size of pions as with neutrons seems likely but is not reported. They have determined RBE values of 1.3–1.4.

Hyperfractionation schedules can be devised using the NSD equation because of the tacit assumption that repair of sublethal damage is complete between fractions. Even with 800 rad, recovery is complete in 24 h and, with doses of the order of 200 rad, in 4 h, so that NSD-type formulae may be justifiably applied to hyperfractionation. In treating glioblastoma, for

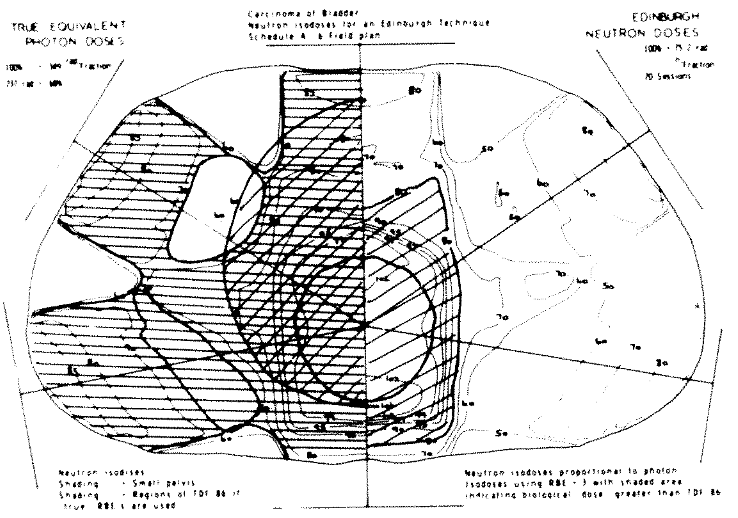

TRUE EQUIVALENT
PHOTON DOSES
Carcinoma of Bladder
Neutron isodoses for an Edinburgh Technique
Schedule A 6 Field plan
EDINBURGH
NEUTRON DOSES
20 Sessions
80
85
50
60
70
Neutron isodoses
Shading - Small pelvis
Shading - Regions of TDF 86 if true RBEs are used
Neutron isodoses proportional to photon
Isodoses using RBE = 3 with shaded area
indicating biological dose greater than TDF 86

FIG. 12.

The right half shows the neutron isodoses from a six-field arrangement to reproduce a pelvic treatment of 200 cGy tumour dose per fraction with RBE = 3. The diagonal shading shows the region of 85 TDF (= estimated bowel tolerance). The left half shows the small pelvis (diagonal shading) and the volume (horizontal shading) receiving 85 TDF (or more) if the true RBEs, as shown in Fig. 11, are used.

instance, I have given to the whole brain 15 doses of 240 rad in 5 days and 20 doses (2 F/day) of 217 rad in 12 days without any clinical indication of neurological damage. These doses were calculated to be less than brain tolerance in accordance with the Sheline formula quoted earlier. Douglas (1982) and Douglas and Worth (1982) consider a therapeutic gain of 1.17 might result from 3 × 0.8 Gy/day instead of 1 × 2 Gy. In 6 weeks (72 Gy) this would be only 60% of tolerance according to the Sheline formula.

Treatment compression and cell birth rate

The above compression of treatment into 1 or 2 weeks was first used because I considered that the cell cycle time of glioblastoma cells could be short and that, between doses in a conventional treatment schedule, significant cell proliferation might occur. I subsequently came across an article (Hoshino et al, 1972) which indicated that the birth rate of glioblastoma cells might indeed be very rapid. Accepting "birth rates" of 1.71 and 0.59 cells/100 cells/h there would be 30 000 tumour cells or 37 tumour cells, respectively, remaining at the end of a 6-week course, as contrasted with 3.4 or 1.5 after 15 fractions in 5 days instead of one cell which might be considered an approximate tumoricidal level of survival.

Tumour survival

This leads on to the question of tumour survival. The relatively radiosensitive tumour, Hodgkin's disease, appears to fit the NSD concept if the equation is used with the data of Friedman et al (1967) but excluding the time factor. Morrison's data on bladder carcinoma (Morrison, 1975) indicate that 100% control can be achieved only with an unacceptable complication rate.

The symbiosis of radiation therapy and radiobiology has been remarkable and profitable. Often, it is held by clinical radiotherapists that radiation biology has not affected the clinical practice of radiotherapy, but there is no doubt that findings in radiobiology influence thinking and will increasingly continue to influence practice. It is recognised that the bigger the dose, the more cells are destroyed, that in most cases tumour doses must be known as accurately as possible and must be as large as possible, and that the region just outside a tumour is the site of a good blood supply so that cells there are more sensitive and require a smaller dose than the tumour itself.

This leads to the concept of target zones. The tumour contains little normal stroma; even the endothelial cells of the capillaries are suspect (Denekamp & Hobson, 1982). Around the tumour, focal deposits occur but normal stroma is in the majority and outside this zone there are microscopic extensions. I think more should be done to determine the extent of these zones. The extension of this concept to shrinking fields is logical. The desirability of condensing treatments when tumours are difficult and the cells may be rapidly dividing is gaining ground. To me, the finding of Spear (1935) that chick fibroblast mitosis was not inhibited by low-dose radiation was important support for low-dose-rate 4π irradiation by implants. The subsequent description by Howard and Pelc (1953) of the $G_1SG_2MG_1(G_0)$ cell cycle and the establishment by Sinclair (1969) of the different sensitivities of a cell at different ages seem to me to provide a further theoretical justification for low-dose-rate radiation. I think that surgical co-operation to implant the tumour bed at the *first excision* of a difficult type of tumour would result in many more cures and much less trouble for all concerned. This is, of course, *intraoperative 4π therapy*. The eventual persistence of "sensitive" tumours which seem to disappear rapidly was a well known contrast in the 1930s with the slower, but permanent, disappearance of relatively insensitive tumours. Hypoxic cells, difficulties in the use of oxygen, the development

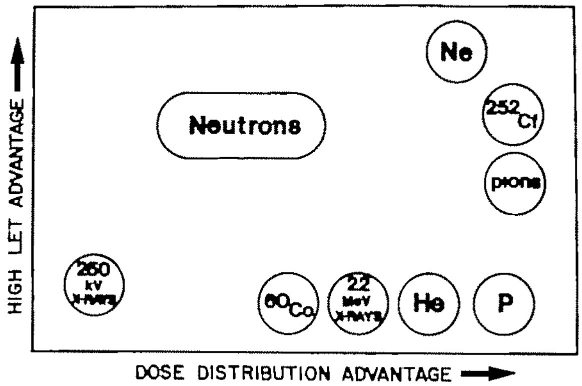


FIG. 13.

Diagram due to E. J. Hall showing relative merits of some ions, pions and fast neutrons (from generators or ^{252}Cf) as compared with helium ions, protons and various electromagnetic radiations.

of sensitisers and, more recently, the radiobiological suggestion of combining the sensitisers with depletion of the protector glutathiene in cells (Epp et al, 1958) has been shown to be profitable. With compressed treatment, misonidazole could be used in higher concentration with less risk of toxic effects because of the shorter periods. This could be tried, for instance, to treat glioblastoma by continuous low-dose-rate treatment to the whole brain with meaningful doses of misonidazole for 24 h up to just below the tolerance level of the normal brain and dispensing during that time with the use of steroids, which are antagonistic to misonidazole (Millar & Jinks, 1981) In view of the possibility that chemotherapy during or after radiotherapy may cause complications (Yarnold et al, 1983), it would seem unjustifiable after a tolerance dose of radiation to give chemotherapy, which has never been shown to eradicate glioblastoma.

High-LET and high-RBE particles have been the subject of much radiobiological research which is gaining some clinical research expression. The use of neutrons has been referred to already Other particles are protons, heavy ions and negative pimesons (pions). The relationship of LET to OER and RBE is well established and their relative potential indicated in Fig. 13.

As with the terminal delta rays of electrons set in motion by photons, the ion density along the track is one important characteristic. Also, the definite range limit of charged particles, the Bragg peak of energy loss and, in the case of pions, the "stars" produced when the particles slow down in the Bragg peak The old idea that it would be ideal to hit cancer cells from inside is reaching fruition in a few ways. Hatanaka is reporting good results (Hatanaka, 1975, Hatanaka & Asano, 1982) from the production of alpha particles in glioblastoma cells by boron-11 capture of slow neutrons, the boron compound ($Na_2B_{12}H_{11}SH$) being taken up in higher concentration by the glioblastoma than by normal brain cells. Monoclonal antibodies targeting on cancer cells with boron 11 is a development of this technique. Recently, the labelling of synkavit with astatine has been used to produce alpha particles in malignant cells of mice (Mitchell et al, 1983a,b).

The use of stilboestrol started about 1937 and immediately the referral of prostatic cancer for radiotherapy was cut off. Now there is a tide in the reverse direction, but the assessment of receptors for oestrogens and for progesterones is promising. Response can be anticipated if the concentration is greater than 11 for oestrogens and 5 for progesterone (normals are less than 3 fM/mg). When the cells remaining are at a minimum would seem to be the best time for irradiation. Chemotherapy can be combined with irradiation, but the evidence so far suggests that chemotherapy before rather than after radiotherapy is to be preferred (Yarnold et al, 1983).

Reference has already been made to the use of implants with surgery. Of course, radiation before and after surgery has been tried, but the finding from the Sloan-Kettering Memorial Hospital of greater effectiveness of radiotherapy if given before 6 weeks post-operatively than after is significant (Vikram & Farr, 1983). There seem to me to be three principles involved in the use of radiotherapy after surgery.

1. The fewer cells there are, the easier it is to kill them all
2. The radiation should be confined to the involved volume.
3. If the cells get locked in scar tissue they are likely to be hypoxic and cannot become oxygenated during a course of treatment as they can by revascularisation in a tumour.

Thus, immediate treatment, as by implant at the time of surgery in the field of operation to give at least a large part of the treatment, seems indicated (Ellis, 1975). An alternative to intraoperative implant in some cases could be the use of an electron beam after healing seems assured, *i.e* 3 or 4 days after the operation. Intraoperative beam therapy also seems logical and is being pursued in some centres (Tepper, 1981).

Hyperthermia as a means of increasing the sensitivity of cancer to radiation has developed recently. I was impressed in 1931 by the conclusion of Reuterwal at Radiumhemmet that tumours in mice were affected by radiation and heat combined to a greater extent than their effects separately added together. For financial reasons it was not possible in 1937 for me to try simultaneous diathermy and radiation for lung tumours, and when I used a Siemens diathermy apparatus at the London Hospital in 1944 I was disappointed that the effect was chiefly to raise the patients' temperatures generally, and decided to wait for a shorter-wavelength apparatus. Since then, the work done on hyperthermia with radiation and with drugs in the treatment of cancer has been intense and, besides techniques for measuring tumour temperature, the effect of the intervals between radiation and heat and vice versa, the relation of effect to temperature and the development of heat tolerance have all been documented (Hall, 1978). The likelihood of poorly vascularised (poorly cooled) areas in tumours is another basis for this method of attacking hypoxic cells.

OTHER GROWING POINTS

Clinical trials

The use of clinical trials is an obvious growing point and a reasonable way of trying to decide on the relative merits and effects of two methods of treatment. I appreciated the urgent need for this kind of trial when, writing an M.D. thesis on ovarian cancer in 1944, it was clearly impossible to reach firm conclusions on many points. Since then the BIR trial on laryngeal carcinoma, initiated during my year as President, has been a successful multicentre trial, comparing three times and five times weekly treatments for their immediate and late effects on tumour and normal tissues. Now the justification for such trials is definitely established. As Cromwell said to the Church of Scotland in 1650, it may be said to objectors wedded to certain methods, "Think it possible you may be mistaken".

Definite recommendations made for clinical trials and the help of a statistician in the designing and meticulous carrying out of a trial result in guidelines (Peto et al, 1976, 1977) which have obvious value. There are so many possible variations, however, in radiotherapeutic procedures that much information tends to be lost. It should be possible to collect reliable and complete data on every patient if the form of hospital notes could be changed so that a check list is the only note completed by the responsible medical officer and stored by a computer for analysis. Results could then be provided easily without so much blood, sweat and tears as formerly. Every patient should contribute to the analysable pool of knowledge.

Chemotherapy and radiotherapy

To me it seems important to decide whether chemotherapy is better given before or after irradiation. A recent prospective study from the Royal Marsden Hospital (Yarnold et al, 1983) showed that with the combined treatment for advanced testicular non-seminoma it was better to give chemotherapy before and not after radiotherapy. Significantly fewer complications resulted. The same has been found (Bleyer & Griffin, 1980) for acute lymphatic leukaemia in children, in that no cases of "leukoencephalopathy" were found in children having no chemotherapy (methotrexate) during or after radiotherapy.

Non-malignant conditions

One part of radiotherapy which has been pruned rather than allowed to grow is the treatment of non-malignant conditions. In some circles this is anathema, and yet few patients so treated by modern methods have evidence of malignant developments. Radioiodine for thyrotoxicosis, strontium 90 for pterygium, X-ray treatment for keloids and irradiation for grafted kidneys are examples. Time was when radiation was used for almost everything for which nothing else could be done, from mental disease and tuberculosis to gas gangrene and plantar warts to shingles. Nowadays, the use of antibiotics has resulted in successful treatment of carbuncles, tuberculosis and all bacterial infections, while fungicides deal adequately with fungal conditions. The use of radiation in very small doses (4 × 50 cGy) to the appropriate nerve ganglia immediately shingles appear is never followed by post-herpetic pain and never shows clinical harm. The treatment of plantar warts by large single doses (1500 cGy) of "contact X rays" to the deepest part of the wart was successful and painless and has never, in my experience, caused any malignant disease. The thyroid in young children, however, is very susceptible to malignant change after radiation.

The development of malignant disease due to radiation does occur, however, but mostly in areas where marked radiation effects in the normal tissue are clinically obvious. Now no-one would consider treating a strawberry naevus in a baby, but I was informed of a patient I treated at about 6 months old for a birthmark over the thyroid by contact X rays (with no filter at 2 cm FSD with compression) who, 30 years later, developed a thyroid carcinoma. I then calculated the possible dose to the thyroid as about 50 rad. The skin was normal. On the other hand a beautiful girl treated by a 2-plane radium implantation (3000 r) for osteoclastoma of the lower jaw at the age of 3 years, before the second dentition had started to erupt, stated 15 years later that she was getting married and would no longer attend for follow-up. Her teeth were perfect.

Radiation protection

Protection is a distinctly growing point. Patients have to be protected from adjacent patients containing "radium" or radium substitutes and the general public must be protected from patients containing radioactive materials. The maximum permissible dose (MPD) for staff is now 0.1 rem per week, a tribute to the efforts of Professor Sievert. In 1931 it was 2 R per week. The protection from X rays was, in my experience, easy; but the protection from various-energy photons, electrons, protons and neutrons is now the business of specialist professionals. Doses to the fingers were not measured until about the 1950s, and even then relatively unsuccessfully. Very large doses were received and had considerable late effects in some cases. In general, any dose to people not being subjected to irradiation for diagnosis or treatment is to be avoided.

The development of afterloading as the consequence of the enthusiasm of the late Ulrich Henschke makes it unnecessary for anyone to receive even the MPD in carrying out 4π therapy. High-dose-rate intracavitary treatment is virtually free from any exposure to staff.

The virtues of afterloading have been emphasised by an international *ad hoc* working party organised by Norman Simon and Margaret Snelling and promoting the use of suitable methods and organisation in developing countries

Information

One of the most obvious growing aspects in radiotherapy and allied subjects is in the literature. It is impossible for any one individual to keep abreast of all developments.

Relevant clinical aspects of cancer, for instance, are now some of the most important growing points affecting or likely to affect the practice of radiotherapy because of increasing knowledge of genetics, immune processes and the natural history of some of the rarer forms of cancer. At present the impact of this type of research is small, although in larger centres such as the Massachusetts General Hospital these developments are of increasing importance. But one can foresee the day when the best treatment for a patient can be recommended by a computer so linked up to accumulated information that when the relevant data in the form of history, examination findings, biochemical data, stage, histology and grade are put in, a recommended treatment management is displayed Indeed, the computer system of the National Library of Medicine of the National Institutes of Health, which is already available at 1800 centres across the United States, was made available in the autumn of 1982 as the PDQ, described as a "New Computerised Database for Physicians treating Cancer Patients". In the Newsletter of the American Society of Therapeutic Radiation Oncology (Vol. 11, No. 3, 1984), the PDQ was reported to be "expanding to include a state-of-the-art statement for each type and stage of cancer", whether standard or investigational, and is ultimately "to be available to physicians via their office computers or word processor equipment, providing a final link in cancer treatment that stretches from laboratory and clinical research to the practising physician".

The failure to feel nodes, to determine an important feature in the history, or other relevant points will, however, be just as important, if not more so, then as at present; and a critical, constructive attitude will still contribute to progress Much can be learned from cases or techniques which are so rare that they have no statistical value but, in general, the use of clinical trials, properly devised, constructed and carried out, will necessarily contribute most to the growth of the science. A close watch should be maintained for many years on the recipients of the numerous cytotoxic, immune suppressant and other biologically powerful drugs.

The past 50 years have seen the development of the Royal College of Radiologists, the Hospital Physicists' Association, Radiation Research Associations, the European Society for Therapeutic Radiation and Oncology, the Cancer Research Society and, in the United States, the American Radium Society, the American College of Radiology, the American Society for Therapeutic Radiology and Oncology and the American Association of Physics in Medicine and its College. Also, protective associations, radiographers' and technicians' societies have all developed in such a way that training and teaching have reached a pitch of sophistication which would have been considered fantasy in 1930 Tribute is due in this country to the early giants who, by initiating the National Radium Centres through the National Radium Commission, did much for the development of radiotherapy in this country and the world, as well as the dedicated radiotherapy which, in 1984, can be used with more knowledge, understanding and wisdom.

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Disc damage above a spondylolisthesis

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ABSTRACT

Fifty-two patients with low back pain and spondylolisthesis at L5/S1 had discograms performed at the L4/L5 level. Retrolisthesis at L4/L5 occurred in 44%, but no direct relationship was demonstrated between the extent of retrolisthesis and either the grade of spondylolisthesis or the presence of disc damage. There was an inverse relationship between the degree of spondylolisthesis and L4/L5 disc damage. Thirty-six patients were assessed for symptomatic pain reproduction during discography. Fourteen (39%) had normal nuclear morphology and no pain induction on injection. Twenty-two patients had disc damage and 11 (50%) had symptomatic pain induced by injection. These results were correlated with the discographic appearances.

Spondylolisthesis, due to a defect in the pars interarticularis, is a well recognised cause of low back pain and deformity. In selected cases, spinal fusion may be the treatment of choice. Some authors have alluded to the fact that intervertebral disc damage may occur at the level above the defect and be a source of symptomatic pain in patients with spondylolisthesis (Simmons & Siegal, 1975, Haraldsson & Willner, 1983). A retrolisthesis is sometimes seen at the level above the spondylolisthesis and this has also been attributed to premature disc degeneration (Laurent, 1958). It is important, therefore, that the state of this disc be established in order to determine the extent of fusion needed at surgery. The aim of this investigation was to study the morphology of the disc above a spondylolisthesis and relate this to the presence of retrolisthesis and symptomatic pain reproduction at this level.

PATIENTS

Fifty-two patients with low back pain and a proven spondylolisthesis were reviewed. These patients had been referred to the Department of Radiology at the Robert Jones & Agnes Hunt Orthopaedic Hospital and all had a spondylolysis at the L5/S1 level, associated with a variable degree of spondylolisthesis. There were 31 males and 21 females with an age range of 13–58 (mean 30.8) years.

METHOD

Lateral lumbar-spine radiographs were reviewed and the severity of spondylolisthesis measured. All radiographs were taken non-weight-bearing. The degree of spondylolisthesis was classified in grades I–IV in increasing order of displacement, according to the method of Meyerding (1938). In this method, the displacement is graded by reference to the four quarters of the superior endplate of the caudal vertebra. The presence of a retrolisthesis of L4 on L5 was noted and measured according to the method of Morgan and King (1957) (Fig. 1). The displacement (ac–ab) was recorded in mm. Discography was performed either in the X-ray department (36 cases) or in the operating theatre (16 cases). When performed in the X-ray department, the postero-lateral approach was used. Care was taken to ensure that the nucleus was adequately filled with contrast medium in order that minor degrees of extravasation through small annular tears could be recognised. In the department, when the examination was performed, the patients were carefully questioned about the nature of any pain induced during the injection and, when present, this was compared with their normal symptomatic pain. Discography in the operating theatre was performed by passing the needle into the nucleus through the anterior annulus.

RESULTS

Age and grade of spondylolisthesis

Of the 52 patients, 37 (71%) had a Grade I slip of L5/S1. Grade II displacement was present in five (10%), and severe slips (Grades III and IV) in 10 (19%). The higher grades were present in the younger patients, nine out of 10 of those with Grade III or IV being in their teens. Those in Grades I and II spanned the whole age spectrum.

Spondylolisthesis and retrolisthesis

Retrolisthesis of L4 on L5 occurred in 23 cases (44%). The extent of the retrolisthesis ranged from 2–8 mm. There was no clear relationship between the degree of retrolisthesis and the grade of spondylolisthesis.

Retrolisthesis and disc damage

Discographically proven damage at L4/L5 occurred in 27 cases (51%). Fourteen of these cases had retrolisthesis of L4 on L5, while the remaining 13 cases had no such displacement. Nine patients with retrolisthesis of L4 had a discographically normal nucleus pulposus (Fig. 1). No relationship was demonstrated between the extent of retrolisthesis and the presence of disc damage.

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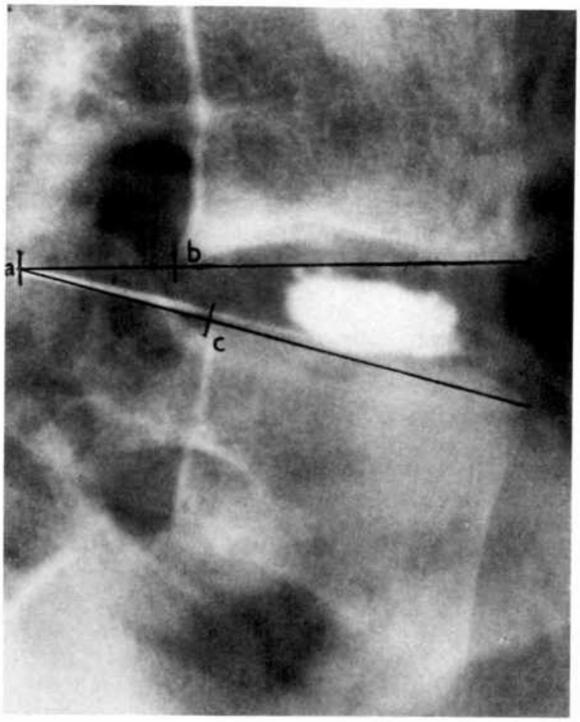

FIG. 1.

An L5/S1 spondylolisthesis with retrolisthesis at L4/L5, in the presence of a normal nucleus: the difference between a–c and a–b is the measure of retrolisthesis.

Spondylolisthesis and disc morphology

There was an inverse relationship between the degree of spondylolisthesis and L4/L5 disc damage, in that only 20% of cases of Grade III and IV displacement had disc damage, whereas 59.5% of Grade I and II cases showed such change (Table I). Analysis of L4/L5 discs of Grade I and II patients by age showed a higher incidence of disc damage in the 30–50-year age range. The age range of those with severe slips was 12–27 years and the two patients with disc damage were 18 years old.

Disc morphology and symptom complex reproduction

Thirty-six patients underwent discography under local anaesthetic (Table II). Fourteen (38.9%) had normal nuclear morphology and no pain was induced by the injection (Fig. 2). The remaining 22 patients had disc damage and, of these, 11 (50%) had their symptomatic pain induced by the injection. The morphological appearance of the 22 damaged discs were divided into two main types: those where the contrast medium was contained within the line of the posterior vertebral margin (Type 1) (Fig. 3) and those showing a herniated pattern with contrast medium contained but extending well beyond the posterior vertebral wall (Type 2) (Fig. 4). The division in this manner indicated that the Type 1 pattern occurred in eight out of 22 and symptomatic pain was induced in only one. The Type 2 pattern was more common, 14 out of 22, and symptoms were induced in 10.

TABLE I

THE RELATIONSHIP BETWEEN THE GRADES OF SPONDYLOLISTHESIS (L5/S1) AND THE MORPHOLOGY OF THE L4/L5 DISC

Morphology of L4/L5 disc	Grades I+II (42 cases)	Grades III+IV (10 cases)
Normal	17 (40%)	8 (80%)
Damaged	25 (60%)	2 (20%)

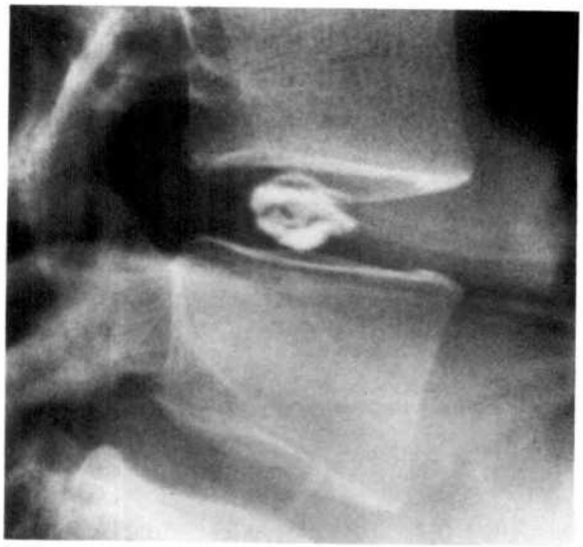

FIG. 2.

Discographic appearance of a normal disc without retrolisthesis.

DISCUSSION

Spondylolysis at the L5/S1 level occurs in 4.4% of 6-year-old children, rising to 5.4% in adults. Spondylolisthesis occurred in 66% of these patients and the overall

TABLE II

SYMPTOM COMPLEX REPRODUCTION AND DISC MORPHOLOGY AT L4/L5

	No. of cases (%)	Normal nuclear morphology (%)	Disc damage Class II	Disc damage Class I
No symptomatic pain reproduction	25 (69)	14 (39)	4 (11%)	7 (19%)
Symptomatic pain reproduction	11 (31)	0 (0)	10 (28%)	1 (3%)

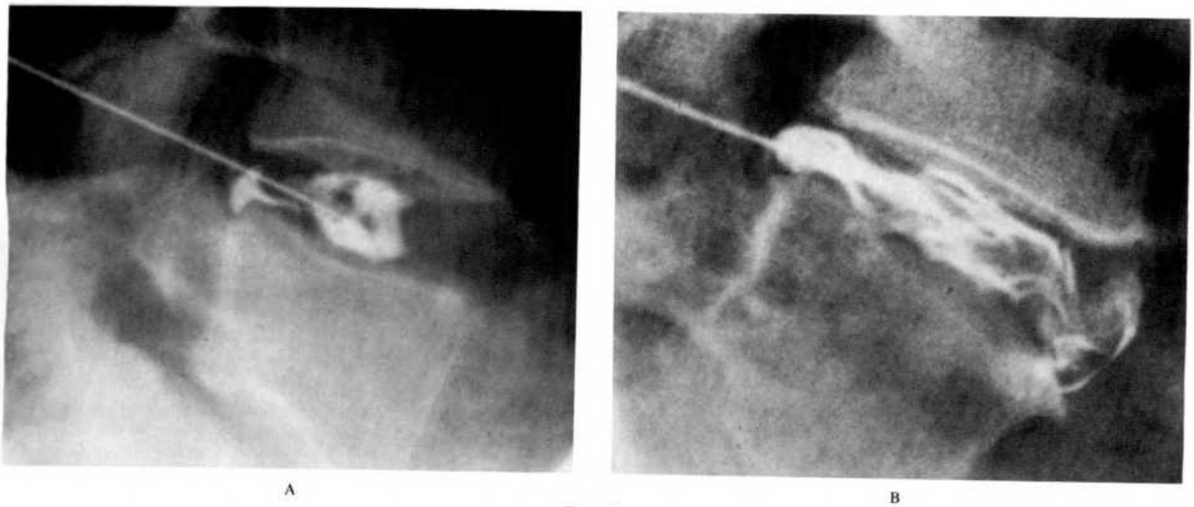

FIG. 3.

Discographic appearance of disc damage at L4/L5. (A) Normal nucleus with small posterior annular tear. (B) Degenerate disc. In both cases the contrast medium is contained at the posterior annular margin and does not extend beyond the normal curve of the posterior vertebral margin.

slip ranged from 0% to 30% (Fredrickson et al, 1984). Most spondylolyses are asymptomatic, although some authors indicate that this condition does predispose to an increased incidence of low back pain (Hult, 1954; Wiltse & Hutchinson, 1964). Degeneration of the disc below the level of the defect is generally observed (Wiltse, 1971). The presence of an L5/S1 spondylolytic spondylolisthesis appears in some cases to produce an L4/L5 retrolisthesis. This has been attributed to degeneration and instability of the L4/L5 disc and is said to occur more commonly above a high-grade slip (Laurent, 1958). In this series, all patients had an L5/S1 spondylolytic spondylolisthesis and nearly half also had a retrolisthesis at L4. We have also shown that although a retrolisthesis is more common above a high-grade spondylolisthesis, there is no correlation between the grade of spondylolisthesis and the degree of retrolisthesis.

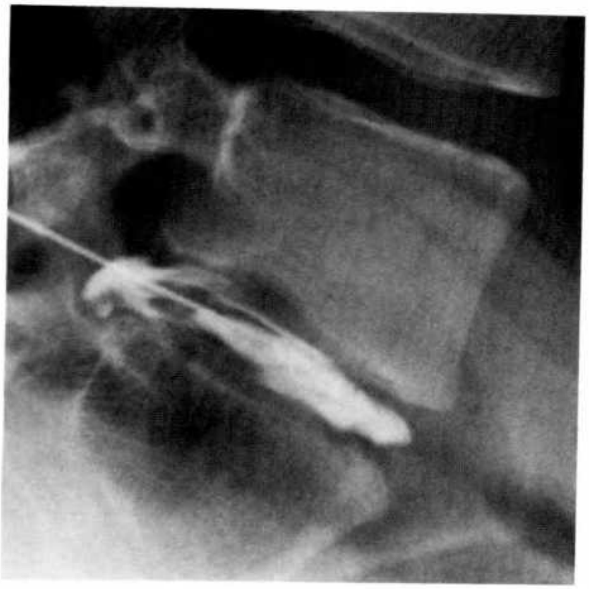

FIG. 4.

Discographic appearances of a degenerate disc at L4/L5. In this case the contrast medium is contained but extends well into the spinal canal. This is a Type 2 pattern.

Spondylolisthesis of L5 on S1 should result in the forward displacement of L4 in relation to S1. The body of L5, however, is separated from the posterior elements by the isthmic defect and the response of L4 to the forward shift of L5 is influenced by the posterior stability provided by the joint capsules and the flaval ligaments between the lamina of L4, L5 and S1 (Nachemson & Evans, 1968). The resisting elasticity of the flaval ligaments will cause a degree of extension at L4/L5 and the overall effect leads to a retrolisthesis of L4 on L5 (Fig. 5) (Penning & Blickman, 1980). The influences of the posterior elements and flaval ligaments on the creation of retrolisthesis at L4/L5 would suggest, initially at least, that the retrolisthesis is independent of disc degeneration. This fact is confirmed by our study in which retrolisthesis at L4/L5 was associated with a normal discogram in nine out of 23 cases. Our results also show no clear correlation between the degree of retrolisthesis and disc degeneration.

The results in Table I show that the L4/L5 disc is more likely to be degenerate in the presence of a less severe L5/S1 spondylolisthesis. A possible explanation lies in the physiological status of the disc. The more severe spondylolistheses tend to occur in a younger age

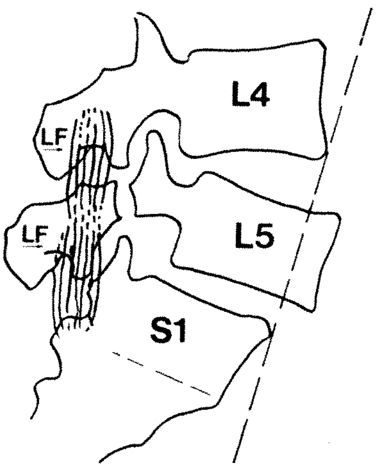

FIG. 5.
The ligamentum flavum (LF) maintains the alignment of L4 with the sacrum causing a retrolisthesis of L4 on L5.

group and it may be that the younger disc is better able to tolerate stress than the older, less plastic disc, which contains less water and more coarse hyalinised fibres. Alternatively, it is possible that the defects in the older patients have been present longer and the discs subjected to longer-term stress, leading ultimately to degeneration. Our results do not, therefore, support those of Laurent (1958).

Several authors (Laurent, 1958; Simmons & Siegal, 1975; Haraldsson & Willner, 1983) have commented on the possible contribution of the cranial disc to the genesis of pain in spondylolisthesis. Macnab (1977) has also indicated that the spondylolytic defect is rarely the sole source of pain in the adult patient and that disc prolapse at the L4/L5 disc in spondylolisthesis is more commonly seen over the age of 30 years. Disc pathology may, however, go unrecognised on plain radiographs and even myelography, especially if vertebral displacement has widened the anterior epidural space. In such circumstances, discography has proved invaluable (Bauer, 1960; Crock, 1976) and has the added advantage of helping to assess the symptomatic potential of the disc damage (Park et al, 1979). In our series, discography and analysis of pain reproduction was carried out on 36 patients.

Symptomatic pain was reproduced by injection into the L4/L5 disc in 11 cases (30%). None of these patients had a normal disc and 10 were shown to have disc damage of Class II type. Of the 25 patients without symptomatic pain reproduction, only four had a similar discographic appearance.

These results do indicate the significance not merely of disc damage but of protrusion of disc material beyond the normal annular vertebral margin. Similar appearances and results have been described by Fraser et al (1983). According to these authors, stretching of the outer annulus is an important factor in the genesis of symptomatic pain in degenerative disc disease.

In conclusion, therefore, in this series of patients with L5/S1 spondylolisthesis, 30% had pain referrable to the L4/L5 level and this information would clearly influence their subsequent surgical management. The study also indicates that retrolisthesis of L4 on L5 does not accurately reflect disc damage at this level in L5/S1 spondylolisthesis. Provocation discogram studies identify the L4/L5 pain source in the older patient. The symptomatic pain reproduction correlates with the presence of protrusion of the damaged L4/L5 disc.

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A comparative study of films and screens for mammography

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ABSTRACT

Ten films and six screens suitable for mammography have been compared for image quality using a realistic quantitative phantom under controlled conditions. The best screen was Min R (Kodak), but three black and white films, Min R (Kodak), Fuji II NC (Fuji) and MR3 (Agfa-Gevaert), scored highly Patient dose was also considered and, with these three films, small gains in image quality were balanced by small increases in dose Medichrome Blue film, however, gave the highest score of all, and did so for a dose that was less than the highest. These results were confirmed on a second phantom of entirely different design.

Following recent results reported from Holland (Verbeek et al, 1984) and Sweden (Tabar et al, 1985) there has been increased interest in screening by mammography for the early detection of breast cancer If small malignant lesions are not to be missed, mammography must be performed to the highest standard, with emphasis on optimum image quality. This requires the identification of the film–screen combination which is best able to demonstrate fine detail and small changes in contrast. At the same time, it is essential to consider patient dose, especially since the patients are normally free of symptoms. In general, the greatest accuracy in recording these features and the lowest dose will not be found in the same film–screen combination. This requires comparisons to be made which are, as far as possible, quantitative, so that in balancing accuracy against dose there is some idea of the benefit and detriment involved.

A few years ago, Min R film and Min R screens seemed to be the most popular single combination in the UK, although in Edinburgh Medichrome Blue film was preferred and, with Min R screens, is currently used here for screening. Edinburgh is one of the four centres in the UK trial of early detection of breast cancer New films and screens are continually becoming available, and it is important to determine what advantages they may have. This paper reports a series of comparisons of films and screens available to us during 1985, using two entirely different test phantoms.

MATERIALS AND METHODS

The films and screens included in this work are listed according to manufacturers in Table I. Although Dupont Lodose films and screens are no longer available, they were used until recently and so were included along with the Ilford screen to assess the improvement in current films and screens

TABLE I

FILMS AND SCREENS INCLUDED IN TRIAL

Manufacturer	Film types	Screen types
Kodak	Min R, NMB, OMA	Min R
Agfa-Gevaert	MR3, Medichrome Blue	MR+, MR50
3M	Trimax	–
Fuji	Fuji NC, Fuji II NC	Fuji
Dupont*	Lodose, Lodose+	Lodose 2
Ilford*	–	Ilford HD

*These products are no longer available

Every film was used on Min R screens, and every screen was used with Min R film. Each film was also used on at least one other screen and each film was used on screens of the same manufacturer, for which it is presumably intended, except for Trimax film. Medichrome Blue was tried on every screen. The resulting combinations include most of those currently used in major British centres. At a later stage, an industrial film was tried without screens.

Test phantoms

The "Barts" phantom (White & Tucker, 1980) was developed for the comparative trial of mammography in Britain conducted by the Hospital Physicists' Association (HPA) (Fitzgerald et al, 1981). It contains several series of opacities, designed to mimic mammographic diagnostic features, which are immersed in an epoxy-resin medium, equivalent to at least some types of breast tissue, being half fat and half water equivalent. Some are designed to test contrast discrimination, while others indicate contrast and resolution combined in various ways. A plan of the opacities is provided with the phantom. Some are always seen on the worst films while others are never seen, even on the best. Scoring is normally a simple matter of counting the opacities visible in each film, though a refinement on this used by us is described later.

The "Wisconsin" phantom is commercially available. The basic material is similar to perspex (lucite) and is not very breast equivalent. There is space within the phantom for up to 12 wax blocks containing "details" (fibres or specks) chosen by the user for each film from a range of 20. Blank blocks of the same material are also available. Once the films are taken, they can be relabelled and scored blind. Scoring can then be in terms of true and false positives and negatives, amongst other possibilities.

X-ray sets and processors

All black and white films were exposed on a Philips Mammodiagnost X-ray set with a 50 mm focus–film distance (FFD) at the Victoria Hospital, Kirkcaldy (VHK) and processed there. All blue films were exposed on a later model of the Philips Mammodiagnost having a FFD of 60 cm, at the Breast Screening Clinic in Edinburgh (BSC) and were processed there.

Both X-ray sets have a focal spot nominally 0.6 mm square and were always used at an indicated 25 kV. Shortly before the trial began, focal spot sizes were checked with a simple pin-hole-in-lead and estimated at 1.1 mm × 1.2 mm at VHK and 0.7 mm × 1.00 mm at BSC. An Ardran-Crooks penetrameter, calibrated at the National Physical Laboratory early in 1985, confirmed the accuracy of the kV indications at least to within 0.5 kV. Both X-ray sets have molybdenum targets and molybdenum added filters of nominally 0.03 mm. With both X-ray sets, films and screens were packed in black envelopes which were automatically evacuated. Earlier work at BSC had shown these to give better image quality than cassettes (Kirkpatrick & Law, 1985).

Exposure control and dosimetry

For both phantoms, manual exposure control was used throughout. Automatic exposure settings used clinically were not always optimal for exposing test films. It was important not to disturb settings since this work was fitted between clinical sessions. Consequently, photographic density varied with the discrete time steps of the manual exposure control, and could not always be arranged to give a precisely specified density.

Film density was checked on a portable densitometer at the time the films were obtained from the Barts phantom. A standard position within the phantom image was chosen, near the centre and clear of details. For black and white films a density of 1.0 was aimed at, while 0.7 was found more suitable for blue films since these are routinely viewed by orange light. Surface dose on the phantom per time set on the exposure control was measured on both X-ray sets with the same 35 ml ion chamber ("Adrian" type) connected to a 37D electrometer (Vinten Instruments). From measured photographic densities at different exposure times, the surface dose needed for density 1.0 (0.7 with blue film) could be estimated with a relative precision of better than 5% for each film–screen combination.

TABLE II

Scheme for two scorers assessing films of Barts test object

Confidence with which detail recorded as seen	Score
Confidently recorded by both observers	1
Confidently recorded by one, not recorded by other observer	$\frac{1}{2}$
Confidently recorded by one, recorded but with less confidence by other	1
Recorded with less confidence by both	$\frac{1}{2}$
Recorded with less confidence by one, but unrecorded by other	0

Results (Barts Phantom)

Using the Barts phantom, each film was scored by each author separately, and the scores combined. When an opacity could be seen clearly by both scorers, or not at all by either scorer, combining scores presented no problem. When only partially seen, or seen with less confidence than usual, scores were assessed using the scheme detailed in Table II. For each film–screen combination on each X-ray set used, five films were taken which were nominally identical. The mean of the combined scores for each of the five films was

TABLE III

Image scores obtained with Barts phantom for various film–screen combinations

Film	Screen					
	Min R	MR+	MR50	Fuji	Lodose 2	Ilford HD
Min R	56.2±0.4*†	50.4±0.3	53.4±0.4	53.8±0.8	55.5±0.6	51.1±0.7
NMB	51.3±1.2*	54.8±1.0*†	–	–	–	–
OMA	51.8±1.7*†	–	–	–	–	–
MR3	55.0±0.5*†	51.6±0.5	55.5±0.5*	–	–	–
Trimax	54.3±0.4*†	–	–	–	–	–
Fuji NC	53.2±0.4	–	–	53.6±0.8	–	–
Fuji II NC	55.7±0.4*†	–	–	54.5±0.5*†	–	–
Lodose	49.3±0.8	–	–	–	48.3±0.3	–
Lodose+	49.4±1.1	–	–	–	48.7±0.5	–
Medichrome Blue	56.9±0.4*†	50.1±0.6*	51.9±1.7	54.4±0.7	55.8±1.2*	52.1±0.7

*Results combined from two X-ray sets.

†Film–screen combinations also checked on GEC X-ray set.

TABLE IV

RELATIVE SURFACE DOSES USING THE BARTS PHANTOM NORMALISED TO 1.0 FOR MIN R SCREEN AND MIN R FILM

Film	Screen					
	Min R	MR+	MR50	Fuji	Lodose 2	Ilford HD
Min R	1.0	1.2	3.1	0.7	1.7	3.0
NMB	0.65	1.1	–	–	–	–
OMA	0.5	–	–	–	–	–
MR3	0.7	1.0	2.4	–	–	–
Trimax	0.65	–	–	–	–	–
Fuji NC	0.6	–	–	0.6	–	–
Fuji II NC	0.85	–	–	0.7	–	–
Lodose	0.95	–	–	–	0.6	–
Lodose+	0.95	–	–	–	0.5	–
Medichrome Blue	0.8	0.45	1.0	0.8	0.55	1.1

calculated, with the standard error on that mean (68% confidence level). Standard errors were generally between ±0.4 and ±1.0.

A set of five films was occasionally rescored after an interval of some weeks or more. Results were always consistent, within the calculated standard errors, indicating at least self-consistency; repeats of two film–screen combinations on a particular X-ray set also demonstrated similar consistency. Cross checks, exposing blue films at VHK and processing at BSC or exposing black and white films at BSC and processing at VHK, showed no consistent, significant difference in scores between the two X-ray sets. Film–screen combinations used in the cross checks are marked † in Table III. Results from both X-ray sets were combined.

The resulting mean image scores for the various film–screen combinations, with their standard errors, are given in Table III. Differences between these means may, at first, seem small, but it must be remembered that some details are always seen and others are never seen. In earlier work (Kirkpatrick & Law, 1981) it was found that at around 25–35 kV, a change of 2 kV produced a change of only 1.0 in mean image score, and the same change could be produced by a change in added filter of 0.14 mm Al. Changes by a factor of 2 in either of these quantities would be expected to produce a detectable change in clinical image quality, so that a difference of 2.0 in phantom image score would also be associated with such a change. The phantom surface doses, corrected to standard film densities as described above, are given in Table IV, normalised to 1.0 for Min R screen and film. The actual incident dose on the phantom is about 7 mGy, giving a mean dose through the phantom of about 1.5 mGy. Patient doses on these X-ray sets are somewhat lower than doses required for this phantom.

DISCUSSION OF RESULTS (BARTS PHANTOM)

Screens

Min R screens still seem to be as good as any. MR50 and Ilford HD screens require higher doses than the others (except for blue film) and give no advantage in image score. The discontinued Lodose 2 screen gave a good result with Min R film and with Medichrome Blue, but a very poor one with both Lodose films. The Fuji screen fails to match the best scores on any of the four films (two of them from Fuji) on which it was tried. The MR+ screen did better on NMB film than on MR3, but still did not match the best.

Films

On Min R screens, four films gave high scores which were very close: Min R, MR3, Fuji II NC and Medichrome Blue, and of these the first and last gave the highest scores of any of the combinations. The relative doses in Table III for these four films on Min R screens show a range of less than ±20%.

Lodose films gave the lowest scores, with NMB and OMA not very much better (except NMB on MR+ screens). Fuji II NC film appears perceptibly better than Fuji NC film, with Trimax in between. The NMB–Min R result was particularly surprising since in 1980 it gave results very slightly better than Min R films and screens (Kirkpatrick & Law, 1981). No explanation for the change since 1980 can be given here, but more recent work with NMB and OMA films has given scores of around 53, suggesting appreciable batch variation in these film types.

Most manufacturers represented here make at least one film and one screen. It was expected that when a given screen was used with the corresponding film the results would have shown some advantage over other combinations in either dose or score, if not in both. This is by no means always the case, and detailed inspection of Tables III and IV reveals some surprises.

Also from Table IV, the ratios of doses for a given pair of films quite often vary from screen to screen and vice versa. This is not at first very surprising since some screens emit blue light and others green, and some films are mainly blue or green sensitive, yet this does not explain away all the apparent anomalies. It seems difficult, therefore, to talk of fast films or screens, but only of fast (or slow) combinations.

Further tests with the Barts phantom

Some of the results were tested by investigating those combinations marked * in Table II on a second X-ray set at BSC. This was a GEC Mammostand II and has only a glass window for filtration (0.5 mm Al nominal equivalent). In other respects relevant to this work, it is very similar to the Philips sets. No change in relative ratings of the film–screen combinations emerged from this. In particular, NMB film again performed better on MR+ than on Min R screens.

Industrial CX film (Kodak) was tried at VHK without screens. The image score was very similar to that from Min R film on Min R screens, but with a dose nearly eight times higher than for the Min R–Min R combination. For that, and many other reasons, the idea was not pursued.

RESULTS (WISCONSIN PHANTOM)

The relative scores on Min R and NMB film on Min R screens were puzzling, as outlined above, and the four best films had shown little difference in score on Min R screens. In continuing to use Medichrome Blue film for all clinical work, Edinburgh seems to stand almost alone in the UK. Also, results from the Barts phantom have, occasionally, been criticised because it is alleged to be insufficiently sensitive.

For these reasons the Wisconsin phantom has been used with Min R screens and the following films: Min R, NMB, MR3, Fuji II NC and Medichrome Blue. X-ray sets, conditions and processing were as previously described. Wisconsin-phantom films were taken by one of us (J.L.) and then randomised and relabelled by a colleague to ensure completely blind scoring. The identity of the blue film as a type was inevitably known to all scorers, but the eight films had been randomised, so that the scoring was equally blind on all film types and for all scorers. For each film type, eight films were taken and all were scored by seven persons (a physicist, a technician, two radiologists and three radiographers, two of whom were recent recruits to mammography) True and false positives and negatives were recorded for each film and each scorer, and weighted: true +ve, +2; true −ve, +1; false +ve, −1; false −ve, −2.

A mean score for each film type was calculated and a standard error calculated from variations among the seven scorers. The results are shown in Table V, which gives the corresponding scores for the Barts phantom for comparison. The ranking order is almost the same for both phantoms. The Wisconsin phantom, as used here, is scarcely more sensitive than the Barts phantom when the statistical uncertainties are considered. It is a less subjective device than the Barts phantom, because the scorer does not know in advance which opacities are present. The similarity of the results from each phantom is a useful confirmation of the reliability of results from the Barts phantom, which is quicker to use.

TABLE V

IMAGE SCORES FOR SELECTED FILMS USED WITH MIN R SCREENS AND ASSESSED ON TWO DIFFERENT PHANTOMS

Film	Mean image score	
	Barts phantom (max score 78)	Wisconsin phantom (max. score 22)
Medichrome	56.9 ± 0.4	13.0 ± 0.75
Min R	56.2 ± 0.4	12.25 ± 0.50
Fuji II NC	55.7 ± 0.4	12.25 ± 1.0
MR3	55.0 ± 0.5	11.25 ± 0.75
NMB	51.3 ± 1.2	10.75 ± 0.75

CONCLUSIONS

It appears that Min R remains the best screen for mammography.

Of the black and white films, Min R, Fuji II NC and MR3 give the best image quality (descending in that order). Of those three, Min R requires the highest dose and MR3 the lowest, though the differences in dose are not large. Thus, small increases in image quality are accompanied by small increases in dose.

An objective choice might be made by screening large numbers of women, using each film and comparing cancer detection rates, but there are severe and obvious problems of both ethics and statistics. The final choice, therefore, has to remain subjective, but anyone using any of these three films might reasonably continue to do so. In view of the relative numbers of cancers detected and cancers induced in a screening programme (Law, 1987) we consider that at present dose levels it is right to give priority to diagnostic accuracy.

Medichrome Blue film, however, gives image quality better than the best black and white film when used with either the Barts or Wisconsin phantom. Moreover, it does this with a somewhat lower dose than Min R film. For anyone with the necessary facilities (processing, orange light viewing) it seems to be, on balance, the best. Its principal drawback, perhaps the only one, is that very few users have any experience of it, and staff transferring to or from centres using it could be at some disadvantage. Even so, in tests with the Wisconsin phantom, two radiographers new to blue film scored as well as two radiologists with years of experience in using it.

Our final conclusion, therefore, is that films and screens which appeared the best available up to around 1980 are probably still the best 5 years later. While reassuring to those who have continued to use them, it is slightly disappointing that no real advance in this period can be identified

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ADDENDUM

Since the receipt of this paper two new films, Ortho M and PE 205, were introduced by Kodak, who invited the authors to assess them on the same basis as the others. This analysis is now appended as an extension to the paper (Ed.)

In addition to comparing films directly, we attempted to answer the question whether any film which gave inferior image quality but at a lower dose than for other films, might show superior image quality when used with a grid, and preferably with doses still no greater than for alternative films.

TABLE VI

IMAGE SCORES FOR FOUR FILMS AND TWO PHANTOMS

	Film			
	Medichrome Blue	Min R	Ortho M	PE 205
Barts phantom (4 5 cm thick)	59.5±0.3	55.7±0.5	52 2±0.9	50 5±0.7
Wisconsin phantom	12.3±0 4	10.0±0.5	8.0±0 4	6.1±0 6

Two series of comparisons were therefore made:

(a) Ortho M and PE 205 against Min R and Medichrome Blue, using phantoms corresponding to breasts of normal thickness, and
(b) Ortho M and PE 205, each with a grid, against Min R and Medichrome Blue, each without a grid, and using a thicker phantom on which a grid might bring some benefit.

The X-ray set used was a Philips Mammodiagnost U. This has a molybdenum target and was operated at 28 kV if a grid was used (to obtain greater penetration through the thicker phantom) and at 25 kV otherwise. The kV settings had been checked with a calibrated penetrameter and were correct within ±1 kV. The grid used was supplied by Philips and is as described earlier (Kirkpatrick & Law, 1985) having 31 lines/cm and a ratio of 5. The principal phantom used was the Barts phantom, supplemented by the Wisconsin phantom. All four films were compared on both phantoms without grid, and then on the Barts phantom increased from its normal 4.5 cm thickness to 6.5 cm and 7.5 cm, the grid being used only on the two new and faster films.

Min R screens were used with all four films as this has been found by us to be clearly the best. It is another Kodak product, compatible with the new Kodak films.

Entrance doses for the Barts phantom have been measured using a 35 ml chamber and 37D electrometer, as previously, and were corrected to correspond to density 1.0 with black and white films and 0.7 with Medichrome Blue film. Surface doses were converted to mean doses through the phantom using the mean percentage depth doses used by us earlier (Kirkpatrick & Law, 1985), namely 25%, 18% and 16% for phantom thicknesses 4.5 cm, 6.5 cm and 7.5 cm.

The image score results using the Barts phantom at 4.5 cm thick and the Wisconsin phantom are given in Table VI. Results on the thicker Barts phantom are given in Table VII and relative doses for Barts phantoms of all thicknesses are given in Table VIII.

The image scores from both the 4.5 cm Barts and the Wisconsin phantoms show the four films in the same order of merit. Since the two phantoms are entirely different, this qualitative agreement seems very

TABLE VII

IMAGE SCORES FOR THICKER PHANTOMS, USING A GRID WITH FASTER FILMS

	No grid		With grid	
	Medichrome Blue	Min R	Ortho M	PE 205
Barts phantom:				
6.5 cm thick	46.3±0 5	44.9±0.4	47 9±0.6	47 2±0.5
7 5 cm thick	46.0±0.6	45.0±0 6	44.5±1 2	44.7±0 7

TABLE VIII

RELATIVE MEAN DOSES FOR BARTS PHANTOMS OF VARIOUS THICKNESSES, NORMALISED TO 1.0 FOR MIN R AND 4.5 CM PHANTOM

	Medichrome Blue	Min R	Ortho M	PE 205
Barts phantom:				
4 5 cm	0.85	1 0*	0 45	0.55
6 5 cm	2.4	2.9	4 2†	6.1†
7.5 cm	5 0	6.0	8.5†	12.3†

*This dose was approximately 2 mGy, averaged through the phantom.
†With grid—remainder without grid.

significant, a point discussed earlier. Barts-phantom films were scored by both authors and Wisconsin films by five people. It is noteworthy that all five scorers (two radiologists, one radiographer and two physicists) ranked the four films in exactly the same order. It appears that, for breasts of average thickness and no grid, the new films are poorer in image quality. On the Barts phantom, quite small changes in image score represent significant changes in detail visibility and the reduction in image score using the Wisconsin phantom is quite marked. The new films do allow a reduced dose, but in the light of estimated cancer detection and cancer induced rates in mammography (Law, 1987) we suggest that image quality is more important than dose, at these breast thicknesses and these doses. The use of a palladium filter with the newer films gave no improvement in image score (Barts phantom) and we had earlier found this with Medichrome Blue film.

Of the two new films, Ortho M is about 20% faster than PE 205 and gave better image scores in spite of its strikingly grainy appearance, and thus seems the better of the two. Its dose advantage appeared even greater with thicker phantoms.

When using a grid with Medichrome Blue film, negligible image improvement was found with a 4.5 cm phantom (see above) but useful gains were found when both 6.5 cm and 7.5 cm phantoms were used. When the newer films were used with a grid, some gain in image score was shown over the older films without a grid at 6.5 cm phantom thickness, but this gain was not maintained with the 7.5 cm phantom. At the same time, the newer films with a grid still require higher doses than the older films without and, at these breast thicknesses, dose is increasingly important. These results are reasonably consistent with those reported by us earlier. The image scores from Medichrome Blue and Min R films with the 4.5 cm Barts phantom match those in our paper quite well. On the Wisconsin phantom they appear rather lower, especially for Min R film, but this is not necessarily surprising (the results were obtained 8 months apart and with some changes in scoring personnel) and need not affect our conclusions.

Conclusion

In conclusion, the newer films do not, in our view, displace either of the older films where normal-thickness breasts are examined without a grid. They do not even offer strong competition to other black and white films such as Fuji II NC, MR3 or Trimax. With thicker breasts, the newer films may have a slight advantage if used with a grid, but at the cost of a higher dose than for the older films without a grid. This raises the possibility of using different films for normal and for thicker breasts, but this might present practical problems in a busy department. On balance, we cannot recommend these films and there remains a need for a faster black and white film than Min R which can be shown to give better image quality. Until such a film becomes available, Min R appears to us the first choice among black and white films for mammography.*

We thank Kodak Limited for supplying us with samples of their new films and inviting us to assess them. We also thank Miss P. H. Blake, Mrs L. Milne, and Dr B. B. Muir for assistance in scoring Wisconsin films.

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*During preparation of this paper Kodak announced their intention to withdraw Min R from the end of 1986—see letter on page 1242 of the December 1986 issue of *BJR.*

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Staging of prostatic carcinoma with radionuclide bone scintigraphy and lymphography

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ABSTRACT

One hundred patients with histologically proven carcinoma of the prostate were examined by radionuclide bone scintigraphy and bipedal lymphography. In 27 cases the bone scintigram and lymphogram were positive, in 16 the bone scintigram only was positive and in 10 the lymphogram only was positive. Although radionuclide bone scintigraphy is the most useful single investigation for detecting metastatic spread from prostatic carcinoma, lymphography should be performed if the bone scintigram is negative, as it is likely to demonstrate nodal metastases in 18% of patients.

Accurate staging of prostatic cancer is required for effective treatment (O'Donoghue et al, 1976). Staging using the TNM modified International Union Against Cancer (UICC) classification (UICC, 1978) depends upon the clinical examination and the results of special investigations. Primary assessment usually consists of a digital examination with prostatic biopsy and an intravenous urogram. Further investigations usually include radionuclide bone scintigraphy and, sometimes, bipedal lymphography.

There have been many reports of radionuclide bone scintigraphy for patients with prostatic carcinoma and the incidence of positive bone scintigrams has ranged from 42% (Shearer et al, 1974) to 40% (O'Donoghue et al, 1976) and 34% (Paulson & Uro-oncology Research Group, 1979).

Lymphography has also been widely used to stage prostatic carcinoma and the incidence of positive examinations has ranged from 81% (Grossmann et al, 1974) to 65% (Paxton et al, 1975) and 52% (Zingg et al, 1974). The wide variation in the incidence of positive lymphograms is probably due to the different criteria used to diagnose nodal metastases in the various studies.

Histological grading of primary prostatic carcinoma for predictive purposes remains controversial. Gleason et al (1974) have shown that metastatic spread, to bone or soft tissues, is more closely related to pathological grading than to clinical staging.

There have been no reports of different imaging techniques being compared with each other, with clinical staging or with histological grading. The aim of this study was to compare the results of clinical staging, histological grading, intravenous urography, radionuclide bone scintigraphy and lymphography in 100 patients with prostatic carcinoma, with a view to simplifying the pattern of investigation.

PATIENTS AND METHODS

One hundred patients with carcinoma of the prostate were assessed by digital examination and clinically staged according to the TNM classification (UICC, 1978) (Table I). All patients had intravenous urograms, radionuclide bone scintigrams and bipedal lymphograms.

The radionuclide bone scintigrams were performed on a Scintronix LFOV gamma camera using an intravenous injection of 555 MBq (15 mCi) of ^{99}Tc^{m}-MDP. Seven images of the skeleton, excluding extremities, were taken sequentially, each image being 3 min long.

Bipedal lymphography was performed using Lipiodol Ultra-Fluid (May & Baker) injected through lymphatics on the dorsal aspect of both feet.

Ninety-two of the 100 prostatic biopsy specimens were graded histologically using the Gleason classification (Gleason et al, 1974).

Criteria for positive results

Skeletal radiography. All patients underwent intravenous urography. The presence of one or more sclerotic areas in the lumbar spine, pelvis or upper femora was considered a positive result.

Bipedal lymphography. A positive result corresponded to a filling defect greater than 1 cm in diameter in an iliac or para-aortic node, or to iliac or para-aortic nodes greater than 2.5 cm in diameter, or to the grossly disordered filling of nodes with no measurable end-points.

TABLE I

TNM CLASSIFICATION OF PROSTATIC CARCINOMA (T STAGING) (UICC, 1978)

T_0	Incidental, no tumour palpable
T_1	Intracapsular, surrounded by normal gland
T_2	Confined to gland. Smooth nodule deforming contour
T_3	Extension beyond capsule ± seminal vesicle involvement
T_4	Involvement ± fixation to adjacent organs

TABLE II

RESULTS OF RADIONUCLIDE BONE SCINTIGRAPHY AND LYMPHOGRAPHY IN 100 PATIENTS WITH CARCINOMA OF THE PROSTATE

Clinical stage	No. of patients	Bone scintigram and/or lymphogram positive	Bone scintigram positive	Lymphogram positive	Bone scintigram and lymphogram positive
T_0	24	9	8	5	4
T_1	8	3	3	2	2
T_2	18	7	6	4	3
T_3	36	22	15	15	8
T_4	14	12	11	11	10
Totals	100	53	43	37	27

Radionuclide bone scintigraphy. The scintigram was graded as positive when there were two or more areas of increased radionuclide uptake which did not correspond to any benign abnormality on subsequent radiographs.

RESULTS

All patients with sclerotic deposits on intravenous urography had positive bone scintigrams.

The incidence of metastases in patients staged clinically as T_3 and T_4 (68%) was significantly higher than in those staged at T_0, T_1 and T_2 (38%) ($p = < 0.005$, χ^2 with Yates' correction) (Table II). Although radionuclide bone scintigraphy produced a higher incidence of positive results than lymphography in all clinical groups, the difference was not statistically significant.

TABLE III

GLEASON (HISTOLOGICAL) GRADING OF 92 PATIENTS WITH CARCINOMA OF THE PROSTATE

Clinical stage	No of patients	2/3/4	5/6/7	8/9/10
T_0	23	4	14	5
T_1	5	1	4	0
T_2	17	2	14	1
T_3	33	2	23	8
T_4	14	0	5	9
Totals	92	9	60	23

The incidence of poorly differentiated Gleason grades (8/9/10) in patients staged clinically as T_4 was significantly greater than in those patients in the other clinical stages ($p < 0.01$, $p > 0.001$) (Table III).

The incidence of metastases in patients whose biopsies were graded 8/9/10 was significantly higher than that in patients whose biopsies were graded 2/3/4 ($p < 0.05$, $p > 0.01$) (Table IV).

DISCUSSION

The series shows that the incidence of metastases was higher in patients with clinically detectable advanced local disease (T_3 and T_4) than in patients with more localised disease (T_0, T_1 and T_2). This was expected, and Paulson and Uro-oncology Research Group (1979) have reported similar results.

A direct comparison between radionuclide bone scintigraphy and lymphography has not been described before. This study shows that both investigations detected metastatic spread in all groups and although radionuclide bone scintigraphy produced a higher incidence of positive results than lymphography, 18% of patients with a negative bone scintigram had a positive lymphogram. These patients would have been considered to be free of metastases if bone scintigrams had been used exclusively.

TABLE IV

GLEASON (HISTOLOGICAL) GRADING AND INCIDENCE OF METASTASES IN 92 PATIENTS WITH CARCINOMA OF THE PROSTATE

Gleason grading	No. of patients in grade	Bone scintigram and/or lymphogram positive	Bone scintigram positive	Lymphogram positive	Bone scintigram and lymphogram positive
2/3/4	9	2	1	2	1
5/6/7	60	32	25	20	13
8/9/10	23	16	14	14	12
Totals	92	50	40	36	26
No grading performed	8	3	3	1	1
Totals	100	53	43	37	27

Histological grading of the prostatic biopsies showed that the patients with advanced local disease (T_4) had more undifferentiated grades than the other clinical groups. Patients whose biopsies were graded as undifferentiated (8/9/10) also had a higher incidence of metastases than those whose biopsies were well differentiated (2/3/4) Despite the association between high Gleason grades, local spread and metastatic disease in this series, lymph-node metastases occurred in all histological grades, and a low histological grade did not exclude the possibility of lymph-node metastases.

Computed tomography (CT) may eventually replace lymphography for the assessment of pelvic lymphadenopathy, as the latter is time consuming and has a small morbidity. The results of CT scanning and lymphography correlate well in patients with carcinoma of the prostate (81%) (Dobbs & Husband, 1985).

Our conclusion is that although radionuclide bone scintigraphy is the most useful single investigation for detecting metastatic spread from prostatic carcinoma, lymphography should be performed if the bone scintigram is negative, as it is likely to demonstrate nodal metastases in 18% of patients.

ACKNOWLEDGMENTS

We would like to acknowledge the support given by our clinical colleagues, in particular Mr P. F. Philip, during the course of this study We are also extremely grateful to Mrs Joyce Harvey for her help in the preparation of the manuscript

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Book reviews

A Manual of Radiographic Equipment. By S. M. Stockley, pp. 304, 1986 (Churchill Livingstone, Edinburgh), £14 95.
ISBN 0–443–02585–1

This book, which is aimed primarily at student radiographers, attempts to cover the topics included in the College of Radiographers' "Equipment for Diagnostic Radiography" examination syllabus. It is divided into two approximately equal parts.

Part 1, which deals with the generation of X radiation, is divided into 11 chapters covering various aspects, from the generation of electrical supply to the filament circuit, high-tension circuit, electrical switching and control of exposure times, to tube rating and safety devices.

Part 2 is concerned with the manipulation and use of the X-ray beam and is divided into 10 chapters covering: fluoroscopy, portable and mobile units, radiographic tables and tube supports, specialised units, accessories, grids and collimation devices, and care of equipment and equipment selection and installations. The very basic chapters on radionuclide imaging and ultrasound fit uncomfortably into Part 2.

The text, which is well presented and logical in approach, has ample explanations and is very well illustrated with bold, clear, easily understandable diagrams. Some may consider the text to be over-simplified. Unlike some publications aimed at a similar market, specific descriptions of specialised radiographic apparatus are not provided. However, the underlying principles of these types of unit are well described and the section on equipment selection and installation is particularly useful. Unfortunately, the review copy is printed on rather coarse paper, permitting diagrams and text from one page to be easily seen while reading the reverse.

I think the book meets the author's aims and will be a very useful acquisition for those wishing to understand more about the basic construction and operation of radiographic equipment. It should certainly find a place in the libraries of radiodiagnostic departments and schools of radiography.

Brian T. Channon

Mammography—A User's Guide. NCRP Report No. 85. pp 178, 1986 (NCRP, Bethesda), $16.00.
ISBN 0–913392–79–0

This monograph from America, produced as a report by the National Council on Radiation Protection and Measurements, is intended as a practical guide for radiologists and radiographers involved with the radiological examination of the breast, as well as physicists and engineers who calibrate, monitor and maintain mammographic facilities.

A considerable amount of well referenced, relevant and up-to-date material is contained in this small book. The opening chapter contains a lucid description of mammographic projections, together with an account of important practical features of screen–film mammography. This includes a detailed appraisal of the use of grids, as well as guidelines for the selection and use of screen–film combinations. A chapter on xeromammography is followed by a summary and comparison of the differences between this technique and screen–film mammography. Further chapters concentrate on image quality and quality assurance. There is a brief description of other breast imaging methods. Procedures are suggested for estimating the radiation dose to the breast, with particular emphasis on the "average glandular dose" as the appropriate quantity for assessing radiation risk from mammography. The report concludes with an extensive analysis of the risk–benefit factors involved in mammography.

The report achieves its stated aims and has the virtues of being both comprehensive and concise. It is recommended to all who are concerned with mammography. In particular, those who are considering the purchase of mammographic equipment will find this book to be very helpful in making the right choice.

G. H. Whitehouse

1987, *The British Journal of Radiology*, 60, 83–87 JANUARY 1987

Technical note

Image non-uniformity in magnetic resonance imaging: its magnitude and methods for its correction

By B. R. Condon, B.Sc., M.Sc., Ph.D., J. Patterson, B.Sc., Ph.D., D. Wyper, B.Sc., Ph.D., M.Inst.P., A. Jenkins, M.B.Ch.B., F.R.C.S. and D. M. Hadley, Ph.D., D.M.R.D., F.R.C.R.

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Image non-uniformity in magnetic resonance imaging (MRI) is a recognised problem when using surface coils but is rarely mentioned with respect to standard head coils, yet it can be a source of error in clinical interpretation of images. Figure 1 demonstrates the type of artefacts due to image non-uniformity for a large, homogeneous solution of water and copper sulphate. The image was acquired in the coronal section using a standard head coil, and vertical (*i.e.* read direction) and horizontal (*i.e.* phase encode direction) pixel intensity profiles through the centre of the image are illustrated. The standard deviation of pixel intensities, expressed as a percentage of the mean value, is greater than ±27% along the 23 cm length of this phantom. Figure 2 demonstrates how these image non-uniformities can affect the sagittal image of a normal volunteer. The display window width and level have been chosen to produce optimum visual contrast at the level of the cerebellum and brain stem but, as a result of image non-uniformity, this produces pronounced loss of signal in the neck and the vault of the skull. Quantitative and even qualitative comparison of pixel intensities across the image in the vertical direction (along the spine for example) are certainly invalid without some form of non-uniformity correction. Image quality assurance measurements, for example using phantoms to determine plane shape and thickness, will also be affected by this problem.

Image non-uniformity may be caused by a number of factors including radiofrequency (RF) transmitter and receiver inhomogeneities, RF penetration, static field inhomogeneity and non-uniformity in the size and shape of the image planes themselves. Attention has been paid by some research centres to correcting for

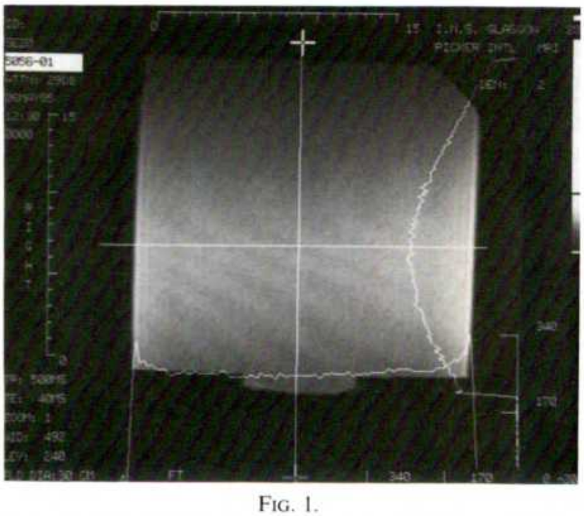

FIG. 1.

Coronal section using a head coil through a uniform phantom showing horizontal and vertical pixel intensity profiles (5 kHz bandwidth). The profiles which appear at the bottom and right hand side of the image are taken along the horizontal and vertical straight lines indicated and are 1 pixel in width.

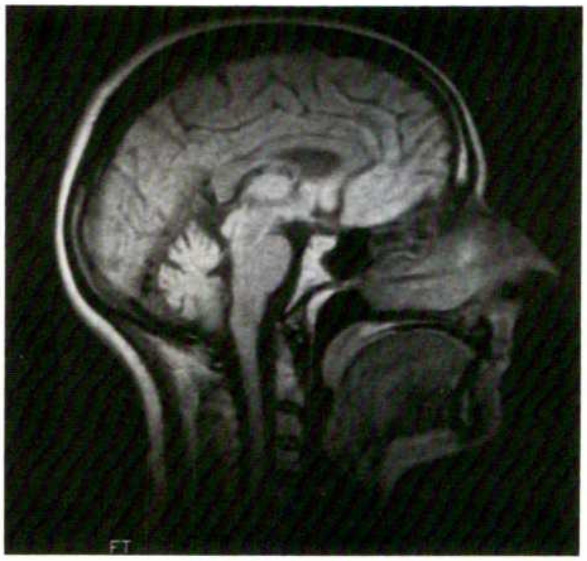

FIG. 2.

Sagittal head section through a normal volunteer with display window width and level adjusted to produce optimum visual contrast at the level of the cerebellum and brain stem (5 kHz bandwidth).

static and gradient field non-uniformities (Sekihara et al, 1984), but attempting to decrease the effects of image non-uniformity by altering the above parameters is beyond the scope and resources of most imaging centres with off-the-shelf MRI systems. In the MRI system at this centre, the major cause of image non-uniformity in the transverse section is bandwidth filtering of the raw data. Increasing the bandwidth decreases the image non-uniformity but at a cost of decreasing the signal-to-noise ratio in the raw data and, consequently, the reconstructed image. Improved frequency filtering of the raw data may decrease non-uniformity without decreasing signal-to-noise ratio but again such an approach is not usually possible for centres with a commercial system. The major source of non-uniformity in the sagittal and coronal sections is due to RF receiver coil inhomogeneity.

In this paper two empirical techniques are described which can be used to decrease significantly the effects of non-uniformity, but which are inexpensive and easy to implement and which do not affect the noise in the raw data.

MATERIALS AND METHODS

All measurements were performed on a 0.15 T resistive magnetic resonance imager and all images were acquired in 128 × 128 format using a 1.0 cm plane thickness and a standard head coil. Initial observations on a variety of phantoms containing homogeneous solutions doped with $CuSO_4$ revealed a common form and magnitude of non-uniformity within the images of the phantoms The form of this non-uniformity was always present, irrespective of the pulse sequences employed (inversion recovery with a spin-echo read sequence or spin-echo sequences both in single or multiple simultaneous slice acquisition), the degree of paramagnetic doping of the solutions and the size or shape of the phantoms. The general form of the non-uniformity was the same irrespective of the imaging section acquired (transverse, coronal or sagittal) but, whereas the magnitude was similar for the coronal and sagittal sections, it was significantly less for the transverse sections. Figure 1 shows the non-uniformity through the coronal section of a cylindrical phantom with diameter 21 5 cm and length 23 cm. This phantom was chosen for the following measurements because, when placed in the imager, it encompasses in all three sections the volume within which the patient's head normally resides. The vertical component (corresponding to the read gradient direction) of non-uniformity takes the form of a "doming out", that is, an increase in pixel intensities towards the centre of the field of view. The horizontal component (corresponding to the phase encoding gradient direction) takes the form of a "dishing", that is, a decrease in pixel intensities at the centre of the field of view, but the magnitude of this is much less severe than the vertical component: the spuriously high pixel intensities at the edge of the image are due to the phase encoding artefact and edge enhancement artefacts (Yamanashi et al, 1984).

It can be demonstrated that a major component of the vertical non-uniformity in the transverse section is due to bandwidth selection by increasing the default value of bandwidth from 5 kHz to 30 kHz The doming effect is decreased in the sagittal and coronal sections (from 27% to 19%) and almost disappears in the transverse section. The main disadvantage of using a larger bandwidth, however, is that the signal-to-noise ratio is proportional to the reciprocal of the square root of the bandwidth (Farrar & Becker, 1971) and so, when changing from a 5 kHz to a 30 kHz bandwidth, the signal-to-noise ratio will decrease by almost 60%. Increasing the bandwidth appears to have no significant effect on the horizontal non-uniformity. The other major source of non-uniformity which affects the coronal and sagittal sections is receiver head coil inhomogeneity, as can be shown by using the same gradients, RF pulses and transmitter coil but substituting the larger standard body coil as the receiver. Under such circumstances this component of non-uniformity is markedly reduced.

Two empirical techniques were developed to decrease this non-uniformity but without the penalty of decreasing the signal-to-noise ratio in the raw data (*i.e.* the free induction decay (FID) data before reconstruction). The first involved determining correction factors for the pixel intensities which were dependent purely on the position of the pixel within the field of view. Starting from the assumption that the pixel values at the centre of the field of view suffered least from the effects of non-uniformity, curve-fitting procedures were used to approximate the pixel values of a phantom image as a function of their displacement from this point. Curves were fitted separately to the horizontal and vertical profile components for each of the three imaging sections. Once the parameters of the curves which best approximated the form of the non-uniformity were determined, it was possible to calculate correction factors for each pixel which were dependent only on their horizontal and vertical displacements from the centre of the field of view.

The second method of correction developed is analogous to the flood source correction technique used to overcome gamma camera non-uniformities in nuclear medicine. A large drum phantom containing water doped with $CuSO_4$, with a diameter of 29 cm and length of 43 cm, which almost completely filled the field of view was imaged in the three axial sections. The mean pixel value of each image was determined and the entire image matrix was then divided by this value. This matrix (the correction matrix) was then used to divide, on a corresponding pixel-by-pixel basis, subsequent images acquired in the same section, which were to be corrected for non-uniformity. The need to use a phantom which fills the field of view for the flood correction is considered in the Discussion section.

The first technique does not introduce any further

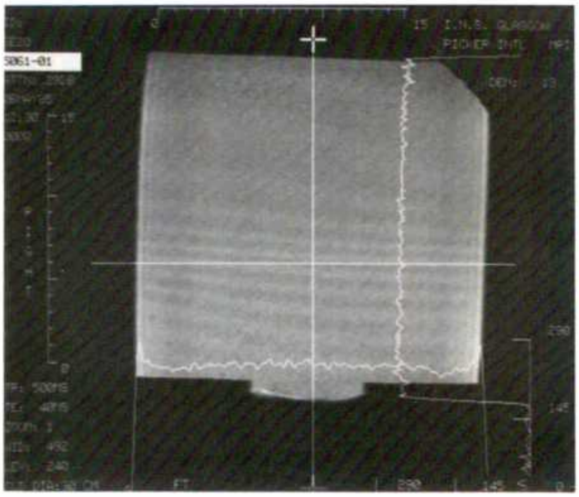

FIG. 3.
The same image as in Fig. 1 after non-uniformity correction using the position-dependent correction factors (5 kHz bandwidth).

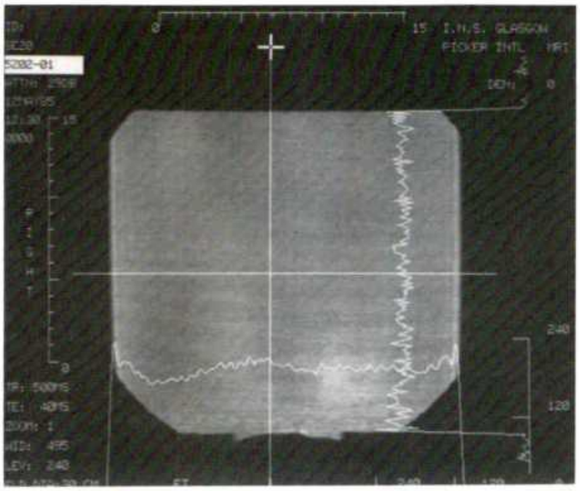

FIG. 4.
Coronal figure of head phantom after correction by flood matrix (5 kHz bandwidth).

noise into the image to be corrected as the correction factor is purely dependent on the position of each individual pixel. The second technique does have the potential to introduce further noise into the corrected image because the pixel values of the "flood" image itself are subject to statistical fluctuations due to the presence of noise. A noisy correction matrix applied to an image will, thus, increase the statistical effects of noise on the pixel values. In order to reduce this, a heavy smoothing operator was arbitrarily chosen and applied to the correction matrix on a line by line basis. The smoothing operation took the form of replacing a pixel value by the mean value of that pixel and the four nearest pixels on that line (*i.e.* a one-dimensional, unweighted, five-point smooth).

In order to assess the magnitude of the vertical and horizontal non-uniformities in corrected and uncorrected images, profiles 10 pixels in width and over 20 cm (170 pixels) in length were taken through the images and the mean and the standard deviation of these pixels were calculated. When analysing horizontal profiles care was taken to ensure that pixels at the edges of the phantom, which had contributions from phase encoding and edge enhancement artefacts, were not included.

TABLE I
REGRESSION COEFFICIENTS (K_H AND K_V) FOR THE THREE AXIAL IMAGING SECTIONS

	Transverse	Coronal	Sagittal
K_H	0.000 026	0.000 020	0.000 013
K_V	0.000 052	0.000 113	0.000 112

RESULTS

In order to establish the optimum correction factors for the first technique, a number of empirically chosen exponential and polynomial curves were fitted to the vertical and horizontal profiles and the regression coefficients determined in each case. Each pixel was then effectively corrected for non-uniformity by dividing by these factors and new images were, thus, produced. Profiles through these images were inspected for uniformity and the mean and the standard deviation of pixel values were calculated. It was found that the lowest degree of non-uniformity was obtained when the correction took the form of:

$$P_{COR} = P/[\exp(-K_V\, y^2)] \qquad (1)$$

for the vertical correction where P_{COR} = corrected pixel value, P = original pixel value, K_V = vertical coefficient and y = vertical distance from the centre of the field of view, and

$$P_{COR} = P/[\exp(K_H\, x^2)] \qquad (2)$$

for the horizontal correction where K_H = horizontal coefficient and x = horizontal distance from the centre of the field of view.

Table I gives the K_V and K_H values for the three imaging sections. Figure 3 shows the effect of the correction after it has been applied to the coronal section image shown in Fig. 1.

Figure 4 shows the result of attempting to correct the image of a coronal section of the uniformity phantom using the "flood" correction technique.

Table II gives a comparison of non-uniformities for images of a phantom acquired in the three axial sections. Non-uniformities are given as the standard deviation of a profile expressed as a percentage of the

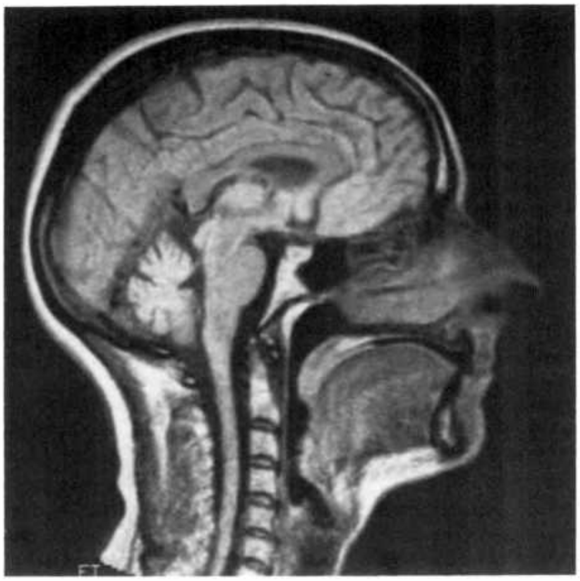

FIG. 5.

Results of applying the positional correction to the sagittal image of a normal volunteer in Fig. 2, keeping the same display window width and levels (5 kHz bandwidth).

TABLE II

IMAGE NON-UNIFORMITY* FOR THE THREE IMAGING SECTIONS

Section	Component	Raw image	Corrections	
			Positional	Flood
Transverse	Vertical	13.1	3.6	4.7
	Horizontal	5.1	3.6	6.0
Coronal	Vertical	27.2	3.0	4.1
	Horizontal	7.6	2.4	5.5
Sagittal	Vertical	26.8	3.0	4.4
	Horizontal	6.8	4.0	7.7

*The figures represent the standard deviation of profile values expressed as a percentage of the mean value over a profile length of 21.5 cm for the transverse section, 23 cm for the coronal and sagittal sections, and a profile width of 10 pixels.

mean value of that profile. Non-uniformities are given for the raw images and for the images after correction by the two techniques.

Figure 5 shows the results of applying the positional correction to the sagittal image of the normal volunteer in Fig. 2.

Both correction techniques were achieved using Fortran programs on the Picker MR computer system (Perkin Elmer 3220). The total run time of the position-dependent correction program was 70 s per image, and of the "flood" correction program, 150 s per image. Marked reductions in run time could be achieved if the corrections were applied at the array processor level.

DISCUSSION

It is not widely appreciated that pixel intensity is not only a function of proton density, relaxation times and sequence timing parameters, but is also largely a function of the position of the pixel within the image due to the effects of non-uniformity. The result of this is that pixel intensities corresponding to signals from tissues cannot be either qualitatively or quantitatively compared if the tissues are vertically displaced in the image. Thus, the signal along the length of the spine will vary, irrespective of the presence or absence of pathology and, indeed, the rapid fall-off of signal towards the periphery of the image may mask or mimic pathology unless some form of image non-uniformity correction is applied.

It must be stressed, however, that "absolute" T_1 and T_2 calculations are not affected by non-uniformity as they are usually calculated from two or more pulse sequences, and so the effects of non-uniformity cancel out. An example of another type of quantitative MRI technique which is used to calculate ventricular and extraventricular intracranial cerebrospinal fluid volumes and which does require a non-uniformity correction is described elsewhere (Condon et al, 1986a,b).

The measurements detailed in Table II are from a phantom which occupies a slightly larger cylindrical volume (21.5 cm diameter, 23 cm length) within the head coil than would be occupied by an adult patient. Even within this volume, vertical non-uniformities within the coronal and sagittal sections (*i.e.* along the patient's long axis) are about $\pm 27\%$. It is worth noting, however, that in certain circumstances parts of the patient's head may lie outside this volume; for example, patients with abnormally large heads or patients who are unwilling or unable to keep their head upright within the centre of the magnet. In such circumstances, and in the coronal or sagittal views, vertical non-uniformities can be up to $\pm 44\%$ of the mean value. Compared with central pixel values, peripheral pixel values can be less than 10% of that value, even in a uniform phantom. Such pixel count fall-offs may mask or mimic underlying pathology.

The non-uniformity correction which is dependent on pixel position appears to work very effectively, especially for the vertical non-uniformity, which is reduced from 26% to 3% in the coronal and sagittal sections. The correction matrix technique also works well in reducing the vertical non-uniformities, but in the transverse and sagittal sections it actually slightly increases the horizontal non-uniformities from 5.1% and 6.8% to 6.0% and 7.7%, respectively. The main reason for this is that the image of any "flood" phantom is, itself, subject to noise and, therefore, extra statistical noise (as opposed to noise in the raw data) is added to the correction matrix and, hence, to the image which is to be corrected for non-uniformity. Fluctuations of the signal from the solution in the drum can also be caused by difficulties in achieving a homogeneous mix of solution in such a large structure. These will also be transferred to the corrected image (Fig. 4). More coarse and repeated smoothing of the "flood" image will reduce noise transference effects but will never totally overcome it and so this technique will always, to some extent, increase the statistical fluctuations in the corrected image. However, as a first-order correction to overcome the gross vertical non-uniformities it may still be adequate.

Problems with mixing are not evident in the phantom used for determining the position-dependent correction factors (21.5 cm diameter). In the vast majority of cases this central section of the field of view easily encompasses the extent of the patient's head. In the small number of cases where either the head is grossly enlarged or the patient's neck is immobile and severely bent, parts of the head may appear outside this central section of the image. While the position-dependent correction approach may still, to an approximation, correct signal in such peripheral pixels, the "flood" correction method cannot, unless those pixels correspond to pixels within the flood phantom. This is because in the normalisation process the pixel contents of the patient's image would be divided by the zero, or near zero, pixel contents corresponding to air around a smaller flood phantom, thus introducing gross signal distortion in the "corrected" image. It is, therefore, necessary to use a larger phantom for the flood correction method, even though inhomogeneities in the mixing of the solution become evident.

The second technique may be applied immediately to any commercial system, whereas the more accurate, and less noisy, first technique will require the calculation of the regression coefficients (K_V and K_H) for each individual system, as bandwidth selection filters and RF receiver coil designs may vary in their effects from system to system. It must be emphasised, however, that neither of the correction techniques affect in any way the noise in the raw FID data, and are purely post-reconstruction corrections as opposed to increasing the bandwidth which, although it may decrease the non-uniformity, will increase the noise in both the raw data and the reconstructed image.

In the uncorrected images it can be seen that the magnitude of the horizontal non-uniformity is much less than the vertical non-uniformity. The positional correction does measurably reduce horizontal non-uniformity, whereas the flood correction technique actually appears to increase it. In common with the vertical non-uniformity, it is symmetrical about the centre of the field of view and not the centre of the phantom, as can be demonstrated by displacing the phantom from the centre. This implies that it is not an RF penetration effect although, clearly, at higher magnetic fields such an effect should be considered. Further work is being undertaken to investigate the source of this non-uniformity.

ACKNOWLEDGMENT

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Book reviews

Selection, Follow-up and Analysis in Prospective Studies. A Workshop. NCI Monograph 57, pp 217, 1986 (US Department of Health & Human Services, Maryland), $17.50. NIH Publication No. 85–2713

This monograph, by the National Cancer Institute, is a report of a conference on prospective studies that was sponsored by the American Cancer Society. It is partly an appreciation of the work of Dr Hammond, with a series of 23 papers in six sessions discussing various issues concerning the methods of prospective studies. In addition to the papers, there are chairmen's remarks for five sessions, and co-chairmen's remarks for another four, together with the discussion at each of the six sessions. These sessions covered: life table analysis, non-occupational cohorts, occupational cohorts, methods of follow-up and classification problems, data analysis, and models of chronic disease.

The material provides a perspective of the contributions of the staff in the American Cancer Society and, at the same time, a review of the changing status of cohort studies in comparison with case-control studies. Though the monograph provides coverage of many aspects of the design, conduct, and analysis of cohort studies, it suffers from the disadvantage of not being structured as a method text on the topic. This reduces its value for the general reader wanting guidance. However, the specialist reader interested in the pursuit of prospective studies will find stimulating examples of method issues in the work. Particular examples of these are the discussions on the contribution to analysis of actuarial approaches, and a paper by Breslow on multivariate cohort analysis.

Some of the discussion of the issues raised is a little disjointed; questions are asked but not resolved in succeeding contributions. Of particular interest is the problem raised by Jablon on whether hazard from radiation should be considered by a relative risk or an absolute risk model He refers to the dilemma now occurring in the US, where two estimates of hazard are available, based on these different approaches This issue provoked a lively discussion, with disagreement as to whether data presently available supported an initiating or late-stage promoting effect from radiation for different malignancies.

Though reasonably priced, this monograph is most likely to find a place in specialist libraries for consultation by those already having appreciable knowledge of the conduct of prospective studies. It is not a work suitable for consultation by the general reader.

M. R. ALDERSON

Sickle Cell Disease. By Graham R. Serjeant, pp. xv+384+index, 1985 (Oxford University Press, Oxford), £35 00.
ISBN 0–19–261543–3

This book is written by one of the great authorities in the field, who has been contributing to the literature on sickle-cell disease for more than 20 years. It succinctly but comprehensively covers most of the problems in sickle-cell disease. From the initial description, by Dr James Herrick in 1910, of "peculiar, elongated and sickle-shaped red blood corpuscles in cases of severe anaemia", to the most recent data on antenatal diagnosis using restriction endonucleases, Dr Serjeant's book makes compelling reading. The book is divided into 37 chapters, all of which are lucidly written and clinically informative

The varied manifestations of sickle disease affecting so many organ systems are dealt with in sequence and the radiological changes presented with particular reference to pathophysiology. The chapter on bone necrosis is of particular interest and the concepts regarding the vertebral "step sign" quite valuable. The reader is led through a particularly useful section of 168 pages, clearly written and illustrated, detailing the severe system effects in each of the major organs. This book is an excellent reference manual; a minor complaint would be the use of black and white rather than coloured illustrations, which was probably dictated by cost. It is extensively referenced with 89 of its 474 pages devoted to a superb bibliography.

The book represents the fruits of years of painstaking effort in the field of sickle-cell disease by Graham Serjeant and, while he is the sole credited author, I suspect that much positive support and encouragement came from his wife, Beryl It is a must for haematologists and radiologists and, with the increasing number of sickle-cell disease sufferers in these islands, should be on the shelves of all medical libraries.

J. T. ENNIS

1987, *The British Journal of Radiology*, 60, 89–90 JANUARY 1987

Case reports

Adrenal-cell carcinoma and rhabdomyosarcoma occurring in father and daughter: "SBLA" syndrome?

By M. J. Tomlinson, M R.C.P. and J. A. Bullimore, F.R.C.R.

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The association of adrenal-cell carcinoma and soft-tissue sarcoma within the same family has been reported and may be an example of a hereditary cancer syndrome. A report is given of a further example of such a family

CASE REPORT

A 34-year-old Caucasian man presented in March 1983 with a 3-month history of cramp in the left leg followed by the appearance of a painless lump He had a 5 cm × 5 cm mass in the left calf which was firm and was not attached to the skin but tethered to deep tissues. Malignant mesenchymal cells suggestive of a rhabdomyosarcoma were apparent from fine-needle aspiration Histology obtained at open biopsy revealed fragments of fibrous connective tissue extensively infiltrated by an undifferentiated, highly vascular malignant tumour with large areas of necrosis and occasional multinucleate tumour giant-cells. The histological appearances and the results of special staining techniques favoured a diagnosis of either an alveolar rhabdomyosarcoma or a clear-cell sarcoma. Electron microscopy confirmed the appearances of an undifferentiated mesenchymal neoplasm (sarcoma).

A lymphogram showed metastatic involvement of the upper para-aortic lymph nodes. A chest radiograph appeared normal, but a computed tomography (CT) scan of the chest revealed several small, left-sided pulmonary metastases.

Chemotherapy comprising vincristine, Adriamycin (Farmitalia Carlo Erba Ltd), cyclophosphamide and actinomycin D in a 3-weekly cycle was commenced, but response was not marked. There was no progress of intra-abdominal disease on a follow-up lymphogram, but a pulmonary metastasis became visible on a chest radiograph Because of persisting discomfort in the calf, and the patient's reluctance to have further chemotherapy at that time, the primary lesion was irradiated using ^{60}Co γ rays The patient then accepted further chemotherapy and received cisplatinum 30 mg IV at 3–4-weekly intervals. He tolerated this extremely well and was able to work fully between treatments. The erythema reduced and the mass became impalpable.

Unfortunately, the pulmonary metastases, which had been static, recommenced growth and became visible bilaterally on a chest radiograph They did not respond to increased doses of cisplatinum or to VP16 and ifosfamide, methotrexate 1 g IV with folinic acid rescue or mitozantrone. In September 1985 recurrence at the primary site was noted.

The patient has a daughter who also presented in March 1983, aged 2 years and 4 months, with a history of rapid growth for the previous 4 months (Height had been in the normal range at a routine 2-year examination) She had developed pubic hair over the same period and had had an acneiform rash for 3 weeks She had excessive underarm sweating and had needed to use deodorants She was also noted to be tearful She had always tended to drink a lot, demanding drinks at night, and had polyuria She had no headaches, had normal vision and had not had any vaginal bleeding. Apart from a febrile convulsion at age 17 months, her past history was unremarkable She was a large child with height and weight on the 97th percentile. (Her father is 5 foot 10 inches and mother 5 foot 4 inches) There was no breast development and no abdominal masses were palpable She had marked clitoral hypertrophy, early pubic hair and rugose labia There was no axillary hair but the axillae were moist.

The initial diagnosis was virilisation due to congenital adrenal hyperplasia, but 17 hydroxy-progesterone levels were normal. There was, however, a high urinary androgen and cortisol level The excretion of androgen was not suppressed by dexamethasone, and the excretion of cortisol was only partially suppressed

A skull radiograph was normal. Her bone age was 6 years and 5 months Intravenous pyelography demonstrated a small area of curvilinear calcification in the region of the right adrenal gland, which did not enhance during the nephrogram stage. An inferior venocavogram showed a round mass, diameter 2 cm, above the right renal pole A CT scan confirmed an adrenal mass with calcification.

A right adrenalectomy was performed under hydrocortisone cover A well encapsulated tumour was found to be arising from the adrenal gland. There were no clinically involved lymph nodes The tumour was excised with its capsule apparently intact Histology showed a lobulated adrenal tumour of variable histological appearance with infrequent mitoses but many tumour giant cells In some areas the border of the lesion was poorly defined The appearance was that of an adrenal cortical tumour, thought to be a carcinoma because of the nuclear pleomorphism and the clinical presentation

As the tumour was believed to be penetrating the capsule, and therefore may not have been completely excised, post-operative radiotherapy to the tumour bed and para-aortic region was advised, and was tolerated well.

She is making good progress, her growth has slowed and the signs of precocious puberty have regressed She has no signs of recurrence on clinical examination or on abdominal ultrasound, and 24 h urinary androgens have remained within normal limits

On enquiry, a further member of the family, the father's maternal aunt, has been treated for carcinoma of the breast, but no other history of familial cancer has been elicited.

DISCUSSION

Kenny et al (1968) described seven cases of virilising tumours of the adrenal cortex, in four of which there was a positive family history of malignancy. This was particularly striking in two families in which four other individuals had cancer. In one family the child's father and sister died of malignant bone tumours, the maternal grandfather died of cancer of the stomach and a maternal great-aunt had breast cancer. In the other family the mother had breast cancer, a maternal aunt had died of a malignant breast tumour, a maternal uncle had died of a brain tumour and a maternal cousin had died of an adrenal tumour. Both children died of metastatic disease from adrenal cortical carcinoma.

An American 8-year nationwide survey (Miller, 1971) of deaths from childhood leukaemia and solid tumours, undertaken to ascertain cancer mortality during childhood in siblings, described two families in which one child had adrenocortical carcinoma and another had rhabdomyosarcoma. The frequency of these neoplasms is so low that only one such occurrence is expected by chance in the United States in 130 years. In one of these families a third child had brain cancer (cell type unavailable) and in the other the mother developed an astrocytoma at 30 years of age (Li & Fraumeni, 1969a). There have been other case reports of adrenocortical carcinoma and brain tumours in close relatives; these neoplasms have also been reported as double primaries (Fraumeni & Miller, 1967; Epstein et al, 1970).

Bottomley and Condit (1968) reported a familial cancer aggregation of sarcoma, brain tumour, breast carcinoma, leukaemia and adrenal cortical carcinoma and suggested that the tendency to develop malignancy in this family was due to an autosomal dominant factor. In some relatives they found an increased percentage of aneuploid cells in cultures of peripheral blood leucocytes (Bottomley et al, 1971). Li and Fraumeni (1969b, 1975) studied similar families and defined the association as a syndrome. They too suggested that inheritance of the syndrome could be due to an autosomal dominant gene with variable expression. However, they thought that inheritance alone was probably insufficient to explain the range of neoplasms seen, and postulated an environmental influence such as an oncogenic virus. Lynch et al (1978) have designated this hereditary tumour complex as the "SBLA" cancer syndrome; S (sarcoma), B (breast and bone tumours), L (leukaemia, laryngeal carcinoma and lung cancer), A (adrenal cortical carcinoma). In their series, 16 tumours were available for pathological review (by light microscopy). Ten showed one or more of the following pathological features: multinucleate tumour giant cells, hypertrophied cells with large amounts of acidophilic cytoplasm, erythrophago-cytosis by tumour cells and three types of cellular inclusions. They suggested the possibility that these findings may have reflected viral injury, although they had no proof of this. They hypothesised that an oncogenic virus acting with a rare autosomal dominant gene had led to the production of highly specific histological varieties of malignant neoplasms (Lynch & Gurgis, 1979).

The family reported in this case report has three members with cancer: the father with rhabdomyosarcoma, his maternal aunt with breast cancer and his daughter with adrenal cortical carcinoma. It is too early to say whether this family will show other features of the "SBLA" syndrome.

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Case reports

Ultrasonic localisation of a non-opaque intravascular catheter fragment

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Vascular access catheters are being used increasingly in both inpatients and outpatients and with the large number of such catheters in use, it is inevitable that complications will occur (Feliciano, 1979). One such complication is the intravascular retention of a broken catheter fragment (Dotter et al, 1971; Huang & Abaskaron, 1984). Since most catheters, such as the Hickman and Broviac catheters, are radio-opaque, radiography or fluoroscopy are usually capable of localising them. However, detachment of non-opaque fragments may lead to serious sequelae. We describe a case where real-time ultrasonography was helpful in preventing complications by locating the catheter fragment which was lying trapped within the right atrium, right ventricle and inferior vena cava. Real-time ultrasonography also aided in the retrieval of the fragment, which was accomplished by a fluoroscopically directed Dormier basket introduced from the right femoral vein.

CASE REPORT

A 25-year-old woman developed an erythematous ulcer on the right cheek. Punch biopsies of the lesion demonstrated necrotising granulomatous inflammation which, on culture, grew *Sporothrix schenckii*. In addition, a subcutaneous nodule was found in the right suprapatellar area which, on biopsy and culture, was also found to be infected with *Sporothrix schenckii*. Amphotericin B was given intravenously, with resolution of the disseminated sporotrichial infection.

To simplify administration of Amphotericin B, a non-opaque intravascular catheter was inserted into the right subclavian vein without complication. A chest radiograph during injection of Renografin demonstrated the tip of the catheter to be at the junction of the superior vena cava and the right atrium. To assess the Amphotericin B therapy, gallium-67 citrate scintigraphy was performed 2 months after the placement of the catheter. This showed considerable resolution of the previously noted abnormalities on the face and leg, as seen on a pre-therapy scan (Moreno et al, 1985).

Since the patient was asymptomatic and had received approximately 2.5 g of Amphotericin B, antifungal therapy was discontinued and the intravascular catheter was removed, when it was noted that a 4–6 in catheter remnant was missing and presumed to be within the vascular system. Conventional radiography of the chest and abdomen failed to locate the catheter fragment. The patient was monitored in the intensive care unit and had multiple episodes of ventricular ectopy and short runs of ventricular tachycardia, suggesting that the fragment was probably within the right heart. This was treated with intravenous lignocaine.

Computed tomography of the upper abdomen did not reveal a catheter fragment but subsequent real-time ultrasonography clearly demonstrated the intravascular catheter extending from the right atrium and ventricle into the inferior vena cava (Figs 1–3). A Dormier basket was placed in the inferior vena cava via the right femoral vein under fluoroscopy. Simultaneously, real-time ultrasonography demonstrated the location of the inferior tip of the catheter within the inferior vena cava. After the Dormier basket grasped the inferior tip of the catheter, the catheter remnant was pulled out of the heart and inferior vena cava into the right femoral vein. Under local anaesthesia, the Dormier basket and the intravascular catheter fragment were removed by a cut-down of the right femoral vein. Once the catheter fragment was located, it was easily retrieved within 30 minutes with use of the Dormier basket. The patient's subsequent hospital course was uneventful.

DISCUSSION

Non-surgical removal of intravascular fragmented catheters is well documented in the medical literature (Ranniger, 1968; Curry, 1969; Henley & Ballard, 1969; Rossi, 1970; Dotter et al, 1971; Block, 1976; King et al, 1976; Millan, 1978; Auge et al, 1984; Huang & Abaskaron, 1984). Location of these fragments prior to

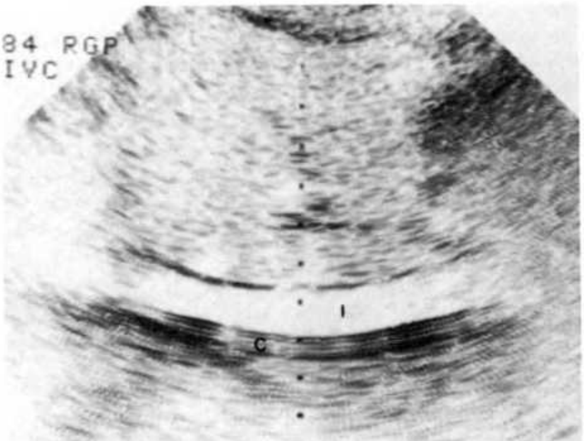

FIG. 1.

Real-time ultrasonography shows a sagittal section through the right lobe of the liver, revealing the full length of the catheter fragment (C) as an echogenic linear structure along the longitudinal axis of the inferior vena cava (I).

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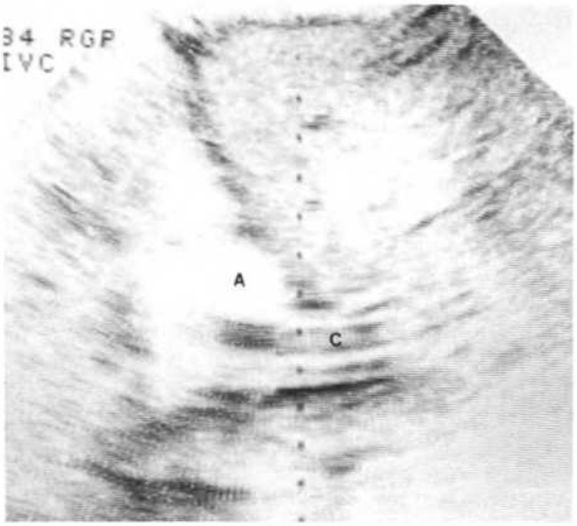

FIG. 2.

Real-time ultrasonography shows a sagittal section through the liver demonstrating the catheter fragment (C) within the inferior vena cava as it enters the right atrium (A).

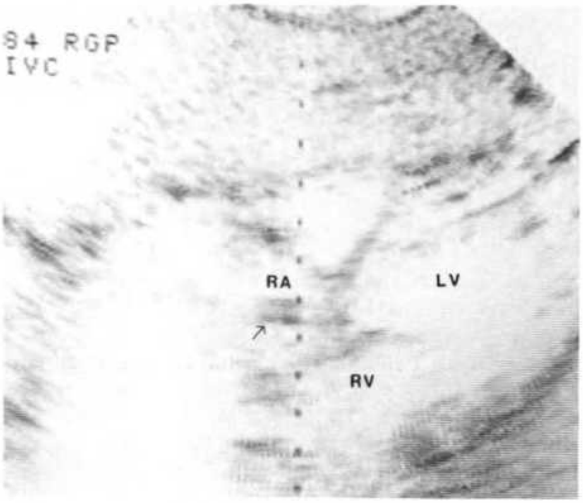

FIG. 3.

Real-time ultrasonography shows a transverse section of the liver angling up from the xiphoid, revealing the catheter tip (arrow) within the right atrium at the level of the tricuspid valve.

retrieval was accomplished by either conventional radiography or fluoroscopy. In our case, a dilemma occurred when the non-opaque intravascular catheter fragment was not demonstrated by the usual radiographic methods or by computed tomography. Real-time ultrasonography, however, readily located the catheter fragment in our patient. The fact that ultrasonography could be brought to the fluoroscopy unit enabled both modalities to be used together to retrieve the radiographically invisible catheter.

The ability to localise catheters with ultrasound has been described previously (Woo et al, 1979; Oppenheimer & Carroll, 1982; Win et al, 1980). The cases described by Win et al (1980) and Oppenheimer and Carroll (1982), however, refer either to the location of a retained left atrial catheter by M-mode echocardiography or ultrasonic localisation of intact neonatal umbilical catheters. Our case is similar to that described by Woo et al (1979), and we conclude that real-time ultrasonography can play a useful role in locating non-opaque intravascular catheter fragments.

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Case of the month

The case of the recalcitrant Welshman

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(Received March 1986)

A 72-year-old retired carpenter presented to his general practitioner in February 1985 with an attack of left renal colic and frank haematuria. He refused hospital admission and settled with antibiotics and analgesia. He also refused investigation at that time, as he looked after an elderly sister. In April 1985 he had an attack of similar pain but with no haematuria on this occasion. He was referred for a urological opinion.

There were no positive findings on clinical examination. Apart from these two attacks he had been well with no relevant past history. He was taking anxiolytics but was on no other drug therapy. Investigations included haemoglobin 16.0 g/dl, white blood cell count 8.3×10^9/l, glucose 5.9 mmol/l, serum calcium 2.27 mmol/l (normal range 2.25–2.60 mmol/l), urea 7.9 mmol/l, creatinine 208 μmol/l, uric acid 0.38 mmol/l (normal range 0.1–0.4 mmol/l). A mid-stream urine specimen yielded no growth. Microscopy showed 0–5 red cells per high-power field.

An intravenous urogram (IVU) was arranged. The control radiograph showed no calculi or other abnormality. Appearances on the 15 min urogram (Fig. 1) and on tomography (Fig. 2) are shown.

What abnormality is shown?

What is the differential diagnosis and how would you investigate the patient further?

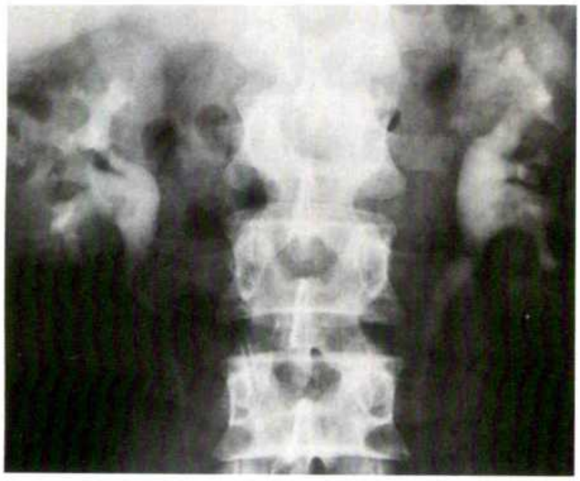

FIG. 1.

Fifteen-minute radiography of the renal area on intravenous urography.

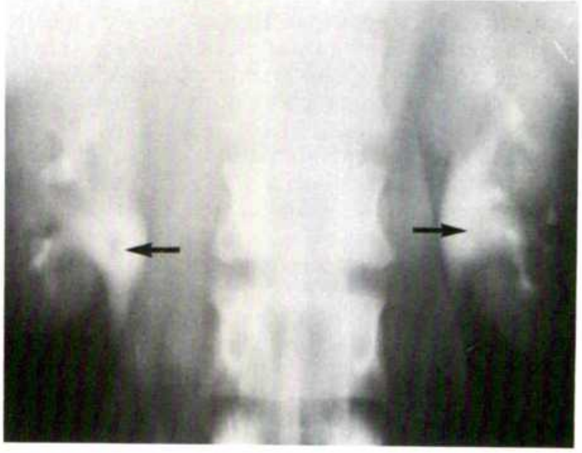

FIG. 2.

Tomography of the renal area.

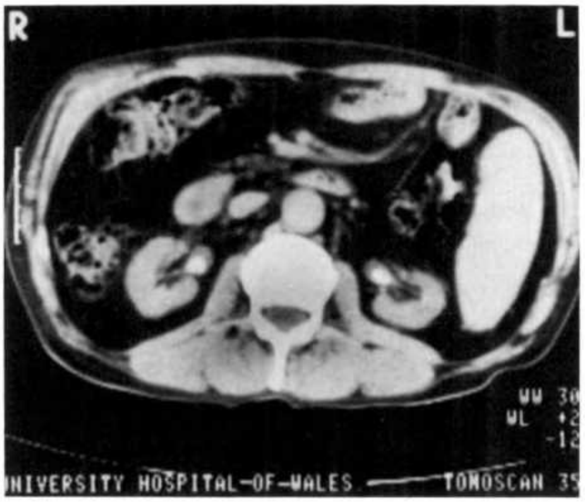

FIG. 3.

Uncontrasted CT scan through the renal pelves showing "pure white" renal calculi.

The urogram shows two filling defects in the renal pelves.

Retrograde pyelography was considered but the patient was unhappy about hospital admission. Computed tomography (CT) was carried out to elucidate further the nature of the filling defects (Fig. 3) and this showed calculi in both renal pelves. The diagnosis of non-opaque stones, probably uric acid, was made. He was treated with Allopurinol, sodium bicarbonate and encouraged to take a lot of fluids. Between April and October 1985 he passed a total of 16 small ureteric stones, several of which were analysed and were composed of uric acid. He has refused radiological follow-up as he feels well.

Non-opaque filling defects shown in the renal pelvis on an IVU have many different causes, but the main differential diagnosis lies between urothelial tumours, radiolucent calculi, blood clot and sloughed papillae. While clinical history, biochemistry, urinalysis and urine cytology may be helpful, further investigation is frequently warranted. Ultrasound, retrograde pyelography, brush biopsy and angiography have been used with varying degrees of success prior to exploratory surgery. With the advent of CT is is now possible to investigate these patients non-invasively and to indicate the most appropriate management.

Radiolucent calculi account for approximately 8% of all urinary calculi. Most are composed of uric acid, while a few are xanthine, matrix or cystine stones. As CT is extremely sensitive in demonstrating density differences, these calculi, which are lucent on plain abdominal radiographs, will appear "pure white" on uncontrasted CT scans (Parienty et al, 1982). Calculi as small as 5 mm have been diagnosed (Segal et al, 1978). There is discrepancy in the reported attenuation values of these calculi, probably due in part to technical factors, such as partial volume effect, but also due to their heterogeneous composition (Parienty et al, 1982). This is not of practical significance as *in-vitro* studies have shown that, while CT attenuation data confirm the order of density of calculi as seen on plain radiography, it is impossible to predict their chemical composition accurately from their CT attenuation numbers alone (Newhouse et al, 1984). Its role is in distinguishing between radiolucent calculi and other non-opaque filling defects of the pelvi-calyceal system. Small calculi may be missed on ultrasound as differentiation from the echogenic pelvis may be impossible if there is no demonstrable acoustic shadowing (Pollack et al, 1981).

Transitional-cell carcinoma presenting as a filling defect on urography may be difficult to recognise on uncontrasted CT scans having a density of 30–40 HU, which is greater than that of urine but less than that of renal parenchyma. It will be more clearly visible on post-contrast scans and will show some enhancement depending on the amount of contrast medium injected and the time of scanning (Parienty et al, 1982). This enhancement will always be less than that of normal renal parenchyma. At the same time it is possible to stage the tumour by identifying extrapelvic spread and metastases to enlarged lymph nodes (Baron et al, 1982). Some caution is necessary as 2% of transitional-cell carcinomas calcify and it may not always be possible to differentiate between transitional-cell carcinoma invading the renal parenchyma and renal-cell carcinoma invading the pelvis.

The density of blood clot in the reported cases is higher than that of renal parenchyma but less than that of non-opaque stones, and shows no enhancement after contrast medium (Parienty et al, 1982). However, attenuation will vary with the age of the clot, being less than that of soft tissue when liquefaction occurs and approaching that of calculi when calcified. Blood clots are often transient, as may be confirmed on sequential urograms. Sloughed papillae would be expected to have an attenuation number similar to that of soft tissue though, if calcified, differentiation from calculi is difficult.

It may not always be possible to be certain about the presence, or the intrinsic or extrinsic nature, of a filling defect in the renal pelvis on an IVU. Extrinsic lesions such as parapelvic cysts are clearly demonstrated by CT, a differentiation that is not always easy by ultrasound as transitional-cell carcinomas are frequently hypoechoic.

Certain points are worth noting in the technique of assessment by CT. It is always necessary to start with uncontrasted scans, as small calculi may be obscured by contrast. Contiguous scans should be performed, using narrow or overlapping slices to examine a suspicious area. Dynamic or rapid-sequence scanning, after contrast medium, will show the pattern of enhancement of a tumour and avoid the possibility of masking a small urothelial tumour by dense contrast-medium excretion.

Intravenous urography is the initial radiological examination in the routine investigation of the renal tract. When filling defects are demonstrated in the renal pelvis and the diagnosis is uncertain, CT should be the investigation of choice. It is definitive in the diagnosis of non-opaque calculi. It will differentiate between extrinsic and intrinsic defects. It will assess the extent of spread of urothelial tumours and, in most cases, sufficient information will be obtained to guide further management.

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Short communication

The relationship between the misonidazole "pre-incubation" effect and misonidazole-induced depletion of cellular GSH

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The misonidazole (MISO) "pre-incubation" effect, whereby the sensitiser-enhancement ratio (SER) is increased following prolonged exposure of cells in hypoxia to MISO, was first demonstrated by Hall and Biaglow (1977). Subsequently, Wong et al (1978) showed that hypoxic cells incubated with 0.5 mM MISO for several hours at 37°C had an increased sensitivity even when subsequently irradiated in air, reflecting a decrease in both the slope and the shoulder of the survival curve. Hall et al (1982) showed that V79 cells exposed to 5 mM MISO in hypoxia became more sensitive to radiation than oxic cells.

Prolonged exposure of hypoxic cells to high concentrations of MISO is known to deplete the cells of their intracellular thiols (Biaglow et al, 1981) and it has been suggested that this depletion is, in part, the cause of the "pre-incubation" effect with radiation (Brown, 1981, Hall et al, 1982). There is also strong evidence to suggest that the depletion of cellular non-protein thiols (NPSH) by MISO is important in its chemosensitising effects (Roizin-Towle et al, 1984).

We have shown previously that prolonged exposure of tumour cells *in vivo* to high doses of MISO did not result in increased radiosensitivity, possibly reflecting an inability to deplete significantly the cells of their NPSH (McNally et al, 1984). In order to try to elucidate further the role of NPSH depletion in the MISO pre-incubation effect, we now present results of a study of the effects of prolonged exposure of mouse tumour cells *in vitro* to different concentrations of MISO in hypoxia. We have measured the SER and the depletion of cellular NPSH following 1 h or 6 h exposure to MISO concentrations of 0.1–1.5 mM.

Methods and Materials

WHFIB mouse fibrosarcoma cells were grown in suspension in alpha modified Minimum Essential medium plus 10% fetal calf serum and antibiotics. For the experiments 4×10^5 cells/ml in logarithmic growth in 50 ml medium were placed in 100 ml water-jacketed spinner flasks, and gassed with 95% N_2, 5% CO_2. All experiments were done at 37°C. One hour after the start of gassing, 5–10 ml of MISO, to give final concentrations of 0, 0.1, 0.2, 0.4, 1.0 or 1.5 mM, were added to the flasks. Cells were then irradiated with 240 kVp X rays either 1 h or 6 h after adding the MISO.

For cell survival studies, after each increment of dose, samples were taken, counted, diluted and plated for colony formation into 5 cm Petri dishes containing 5×10^4 feeder layer cells. The dilutions were such that the MISO was diluted to insignificant levels. The plating efficiency was 90%. Except for the two highest MISO concentrations, all experiments were performed at least twice (see below).

In parallel experiments, intracellular GSH levels were measured in two ways. The first was by the high-performance liquid chromatography (HPLC) method developed by Minchinton (1984). The second was to measure cellular fluorescence in a flow cytometer following incubation of cells with monobromobimane (MB). The procedure was essentially as described by Durand and Olive (1983). 4×10^5 cells were washed once with PBS and then suspended in 10 ml PBS containing 10 μg/ml MB, and incubated at 4°C. The cells were analysed 15–60 min later in an Ortho Systems 50 cytofluorograph. Excitation was with 100 mW 360 nm light from a 4 W argon laser, with fluorescent light collected above 480 nm. At least 2×10^4 cells were analysed at each time and the mean fluorescence of the population calculated. Relative changes in GSH could then be expressed in terms of relative changes in this mean. For each MISO concentration, at least four repeat experiments were performed.

Results

Figure 1 shows survival curves for WHFIB cells exposed to 1.5, 1.0, 0.4 or 0.1 mM MISO for 1 h or 6 h. The two highest concentrations were toxic at 6 h, reducing the plating efficiency to 5% and 25%, respectively. Because of this, only one experiment was done at these concentrations. In all cases the MISO enhancement ratio increased following the longer exposure time. There was no effect of MISO in air.

The SERs for the above concentrations of MISO and for 0.2 mM MISO (curves not shown) are given in Table I. In every case there was a significant increase in the SER following a 6 h exposure to MISO relative to that for a 1 h exposure. The SERs were calculated as follows. First, an exponential line was fitted by the method of least squares for each set of conditions individually, using survival values below 10^{-1}. A mean extrapolation number was then calculated for each data set (*e.g.* air, nitrogen and nitrogen plus 0.4 mM MISO for 1 h or 6 h). Exponential lines were then recalculated using this common extrapolation number and slope ratios (relative to that for cells in hypoxia alone) were calculated together with their 95% confidence limits (the SER).

Figure 2 shows the change in NPSH at 6 h relative to that at 1 h for the different MISO concentrations determined either by HPLC or by flow cytometry. The errors, where shown, represent two standard deviations of the mean for at least four determinations. At 1 h there was no significant effect of MISO on the GSH content of the cells. For instance, for 0.4 mM MISO, the GSH level at 1 h relative to that at the time of adding the MISO was 0.98 ± 0.31 (two standard deviations) and for 1 mM MISO it was 1.11 ± 0.22 (control cells contained approximately 6–10 fmol GSH/cell). Qualitatively, the two

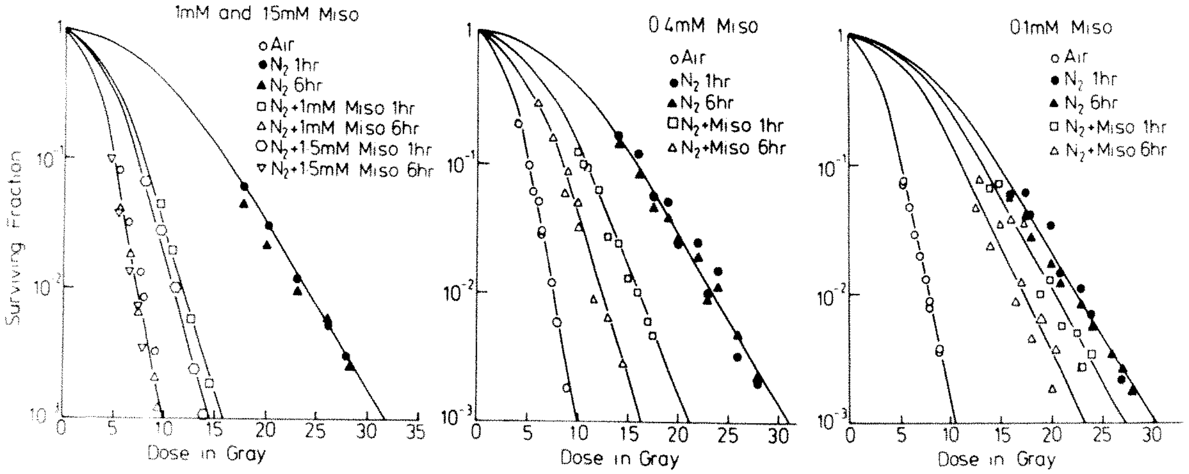

FIG. 1.

Survival curves for WHFIB cells incubated with different concentrations of MISO in hypoxia for 1 h or 6 h prior to irradiation. Only one experiment is shown for MISO concentrations of 1 mM and 1.5 mM because of toxicity at 6 h. Data from two experiments are shown for 0.4 mM and 0.1 mM MISO.

methods of estimating relative GSH content give the same result, no significant effect for MISO concentrations up to 0.4 mM, but a marked depletion of cellular GSH at higher concentrations.

An example of the changes in fluorescence caused by MISO is shown in Fig. 3. The upper row is for exposures to 0, 0.4 and 1.5 mM MISO for 1 h and the bottom row is for a 6 h exposure. There was a small decrease in the mean fluorescence for cells exposed to nitrogen for 6 h relative to those exposed for 1 h. There was no difference for cells in 0.4 mM MISO relative to nitrogen at 6 h, but a marked decrease in the mean fluorescence for cells exposed to 1.5 mM MISO for 6 h.

DISCUSSION

The "pre-incubation" effect we have demonstrated in WHFIB cells is similar to that first demonstrated by Hall and Biaglow (1977), namely a reduction in the D_0 after prolonged exposure to MISO relative to that for a 1 h exposure. In none of our studies did MISO have a significant effect on the shoulder of the survival curve. In contrast, Wong et al (1978) found that MISO could also reduce the shoulder. At 1 h there was no fall in the average GSH content of the cells. It is possible that specific pools of GSH were depleted; nevertheless, it is likely that at 1 h the enhancement ratio reflects primarily the oxygen mimetic free radical mechanism of radiosensitisation.

Roizin-Towle et al (1984) reported that a 3 h treatment of hypoxic V79 cells with 5 mM MISO reduced the non-protein

TABLE I

MISONIDAZOLE ENHANCEMENT RATIO AT 1 H OR 6 H (±95% CONFIDENCE LIMIT) FOR WHFIB CELLS AT 37°C

MISO concentration (mM)	SER 1 h	SER 6 h
1.5	2.17±0.10	3.38±0.18*
1.0	2.01±0.10	3.28±0.16†
0.4	1.48±0.05	1.94±0.13
0.2	1.23±0.08	1.63±0.09
0.1	1.12±0.06	1.32±0.08

*Plating efficiency 0.05.
†Plating efficiency 0.25.

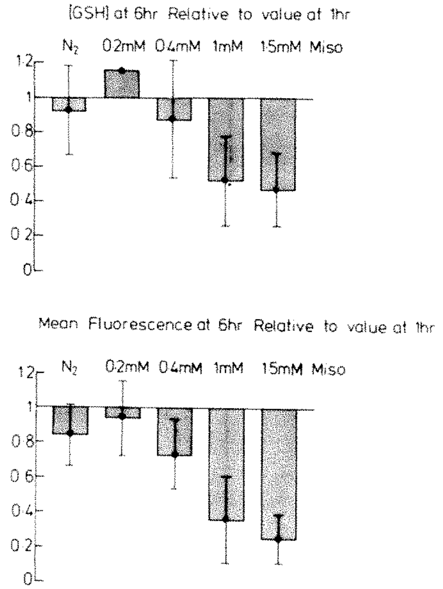

FIG. 2.

Changes in GSH induced by a 6 h exposure to MISO in hypoxia relative to values at 1 h. Top, as measured by HPLC; bottom, as measured by flow cytometry. Error bars are two standard deviations of the mean for at least four determinations.

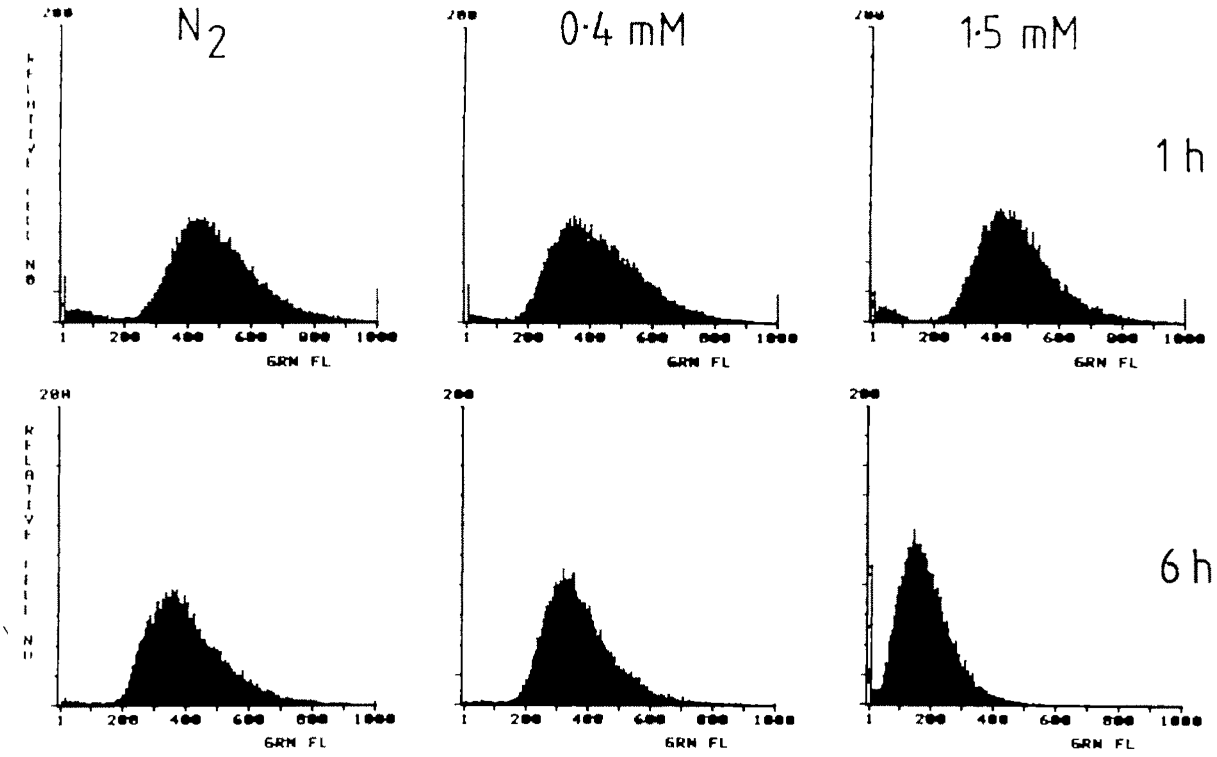

FIG. 3.

Fluorescence profiles for WHFIB cells stained with 10 μg/ml monobromobimane after hypoxic treatment with MISO for 1 h or 6 h (details in text).

thiol level to less than 5% of control values. Anderson et al (1985) found that in bacteria a 4 h exposure to 1 mM MISO reduced the NPSH level to about 6% of the control value. We have found that a 6 h exposure to 1.5 mM MISO reduced the level in WHFIB cells to approximately 40% of control values (Fig 2). However, this treatment was very toxic, reducing the plating efficiency to less than 10%. MISO concentrations of 0.4 mM and less had no significant effect on cellular non-protein thiol levels or on fluorescence as measured in the flow cytometer (Fig 2). The error bars for 0.4 mM MISO (Fig 2) are such that there could have been a small decrease in the GSH level at 6 h relative to that at 1 h to, at most, about 80% of the 1 h value. There is also an indication that simply gassing cells in hypoxia for 6 h may have reduced the GSH level slightly. It seems unlikely to us, therefore, that the increased SER at 6 h for 0.4 mM MISO is due to GSH depletion. Certainly, this is not the case for 0.2 mM MISO, which had no effect on GSH levels (Fig 2) or 0.1 mM MISO (data not shown).

Our observation, that there was an increase in the SER after a 6 h exposure to low concentrations of MISO in the absence of significant GSH depletion, implies that the MISO pre-incubation effect is not exclusively a reflection of the ability of MISO to deplete cells of their NPSH. Anderson et al (1985) came to a similar conclusion measuring the pre-incubation effect in bacteria. The fact that prolonged exposure of cells in hypoxia is necessary suggests that reductive metabolism of MISO may be important, perhaps in producing MISO metabolites which can form adducts with DNA (Varghese & Whitmore, 1980). These might then interfere with chemical or biochemical repair of radiation damage. Misonidazole can prevent repair of potentially lethal damage in plateau phase cells (Brown et al, 1984). However, we have found that it does not prevent recovery from the potentially lethal damage that is expressed when cells are incubated in anisotonic medium after irradiation (McNally & de Ronde, unpublished data). It therefore remains to be demonstrated what the nature of the damage and/or repair process is that may be affected by prolonged exposure of cells in hypoxia to misonidazole, and hence lead to the pre-incubation effect. Whatever it is, depletion of cellular NPSH does not seem to be a significant factor at low MISO concentrations (less than 0.4 mM).

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

A rational approach to the investigation of the gallbladder

The Editor—Sir,

We read with interest the article by Watson and Wild (1986), as we have been carrying out a similar study in Aberdeen. During 1983–84, every person attending the outpatient department of the Aberdeen Royal Infirmary for an oral cholecystogram (OCG) also had an ultrasound scan of the gallbladder. We found that approximately 5–6% of patients with an apparently normal OCG had gallbladder abnormalities on ultrasound.

We do not screen patients who have had an OCG and perhaps some of our "normals" would have fallen into the "Group 3" category as described by Watson and Wild and would, therefore, have had ultrasound examination. Nevertheless, we feel a significant number of people in "Group 1" who would not have had an ultrasound scan could, in fact, have gallbladder abnormalities.

Yours, etc.,
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(*Received July 1986*)

Authors' reply

We were pleased to see that another group has been looking into the problems of gallbladder investigation. We feel, however, that their comments are invalid, as their method of carrying out oral cholecystography is not ideal. This gives us a further opportunity of stressing the importance of a properly conducted oral cholecystogram. It is our opinion that this must include fluoroscopy of the patient in the erect position with the addition of multiple spot filming with a horizontal beam.

Yours, etc.,
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Clinically derived dose–effect relationship for hyperthermia given in combination with low-dose radiotherapy

The Editor—Sir,

I have reframed from an earlier reply to van der Zee et al (1986) because of the publication of the paper regarding the mathematical basis of synergism between heat, electromagnetic radiation (EMR) and X-ray therapy (Holt & Stanford, 1986). It describes the basic reasoning behind my treatment schedules. Dr Alan Nelson and I have treated in excess of 6000 patients with combined therapy using non-EMR heating or EMR as the ionising radiation adjuvant. The temperatures were measured in most of the first 1000 or so patients between 1973 and 1975. Either telethermometry using an AGA Thermovision unit (for superficial cancers) or a platinum thermocouple was used. The latter was inserted into a pre-placed nylon sheath at the termination of the EMR therapy, and a cooling curve plotted and extrapolated back to the instant of cessation of EMR radiation. Three of the 11 patients reported by Holt (1980) were surveyed: two with neck nodes using infra-red thermometry and one with an inguinal mass using the thermocouple. No temperatures exceeding 39.4°C were induced in these cancers.

I must emphasise that the results quoted by Holt and Stanford (1986) for treating head and neck cancers are exclusively from patients who had EMR and X-ray therapy in that order. When treatment was given in reverse order, as van der Zee et al (1986) had done, Dr Nelson and I could not obtain similar results. Neither could we obtain satisfactory immediate resolution and/or short-term survival using non-EMR heating or EMR heating at other than 427–438 MHz either before or after X-ray therapy.

It is my considered opinion, therefore, that when cancer is treated with an X-ray/hyperthermia sequence, its lethality, while related to the X-ray dose as usual, is also dependent upon the temperature and length of heating time. Such a regimen demands maximum tolerable thermal enhancement for its success. The reverse regimen, simple (non-EMR) hyperthermia followed by X-ray therapy, produces similar objective and subjective responses to the X-ray therapy/hyperthermia sequence. Again, lethality appears to be related to X-ray dose, temperature reached and length of heating time.

Irradiation at 434 MHz quickly followed by X-ray therapy produces responses so different from any other regimen as to suggest a non-thermal mechanism. If 434 MHz (frequently inducing a low temperature rise, often well below 41.8°C) plus X-ray therapy produces a survival in head and neck cancers three times as good as that from X rays alone or from an identical (or larger) dose of X-ray therapy preceded or succeeded by simple hyperthermia to 41.8°C, then only a non-thermal EMR-induced sensitisation could account for the difference. It appears, to me, unrealistic to expect a non-thermal EMR radiosensitising effect to be discovered when using the sequence X-ray therapy followed by EMR therapy.

For these reasons I abandoned routine thermal measurements in 1977 and now solely use the regime of 434 MHz EMR delivered before 150–180 cGy (rads) X-ray therapy on two or three occasions per week.

Yours, etc.,
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(*Received June 1986 and in revised form August 1986*)

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A simple design for an accurate uniformity phantom

THE EDITOR–SIR,

The uniformity of gamma-camera sensitivity is an important parameter affecting the quality of gamma-camera images, and all current gamma-camera designs exhibit non-uniformities of the order of a few per cent across their field of view Consequently some type of uniformity correction is applied to the acquired data and the importance of the accuracy of this is particularly crucial in emission computed tomography (ECT), where Rogers et al (1982) have shown that uniformity of response to within 1% is required

Such an accurate uniformity correction is not obtainable using the commonly available ^{57}Co uniformity phantoms, which typically are only specified to be uniform to within ±4% over regions 25 mm in diameter. Most ECT gamma-camera users have, therefore, used refillable perspex phantoms filled with a well mixed solution of ^{99}Tc^{m} in order to achieve the necessary correction

A major problem with these phantoms is the possible distension of the phantom when it is filled (or if its temperature changes). This has been investigated by Mills et al (1983), who found a variation in uniformity of ±10% due to a bowing out of 3 mm at the centre of such a phantom. In addition, most of these phantoms are constructed from standard perspex sheets for which the manufacturer's tolerance on thickness is also ±10%, thus giving a further possible source of non-uniformity Both these problems can be overcome by accurately machining the phantom out of a solid block of perspex and taking care with the filling procedure to avoid distension (Mills et al, 1983) This solution is expensive and requires accurate specialist machining over the entire area of both surfaces of the top and bottom plates of the phantom in order to ensure uniform thickness

The solution we have used to overcome this problem for a Technicare Ω500 gamma camera is to construct a rectangular phantom from two plates of float glass (605 mm × 450 mm) separated around their edges by a stainless-steel frame. The plate separation provided by the frame is 40 mm and the frame was machined to an accuracy of better than ±0 3 mm, which is well within the capability of most medical physics department workshops. The float glass, obtained from a local glass merchant, is 6 mm thick and has a tolerance of ±0.3%. In addition, it can be shown that the glass deflects by less than 0.2% of the phantom thickness even if the full weight of the phantom is taken in the centre of one plate. The glass was fastened to the frame using Araldite 2003 adhesive and a filling channel inserted through the upper glass plate beyond the field of view of the gamma camera.

This phantom proved simple to manufacture and construct and has now been in routine use for over 2 years, during which time it has proved entirely satisfactory.

Yours, etc ,

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(*Received August 1986*)

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Proceedings of The British Institute of Radiology

Progress in tumour radiobiology: radiobiology work-in-progress

Abstracts of papers presented at the above meeting, held at 36 Portland Place, London W1N 4AT on May 16, 1986

Chairman: Dr S. B. Field

Hoechst 33342 as a vascular marker in tumours, by K. A. Smith, S. A. Hill and J. Denekamp
An autoradiographic approach to measuring regional blood flow in animal tumours: preliminary results, by G. M. Tozer
Studies with a potential anti-melanoma agent: an α-emitting radioanalogue of methylene blue, by E. Link, I. Brown, R. N. Carpenter and J. S. Mitchell
Are tumours growing in irradiated beds more hypoxic? by M. Penhaligon, D. Courtenay and R. S. Camplejohn
Site differences in the radiation response of RIF tumours in anaemic mice, by H. C. Walker, R. Myers and S. Hornsey
A lymph-nodal TD_{50} assay for metastatic cells, by B. Dixon and D. A. Bagnall
Comparative radiobiological properties of human tumour cell lines, by G. G. Steel, J. M. Deacon, G. M. Duchesne, L. R. Kelland and J. H. Peacock
The radiation response of a human colon adenocarcinoma grown in monolayer, as spheroids and xenografted in nude mice, by C. West
The effects of radiation on multicellular spheroids derived from human tumours of diverse types, by T. E. Wheldon, A. Livingstone, L. Wilson, J. Russell and J. Adam

HOECHST 33342 AS A VASCULAR MARKER IN TUMOURS

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The vascular networks of two spontaneous murine tumours have been investigated using the fluorescent DNA stain, Hoechst 33342. Mice were injected intravenously with 0.01 ml/g of a 2 mg/ml or 4 mg/ml solution of the stain and killed 1 min later. From cryostat sections, blood-perfused spaces in tumours were identified as infrequent "halos" of fluorescent cells. Estimates of the tissue areas exposed to the drug (*i.e.* the functional vascular volume) have been calculated using point scoring and the distribution of vessel diameters measured over a range of tumour sizes.

The vascular volume was similar in both tumour types (2–4%) and agreed with values obtained using a ^{51}Cr-labelled RBC technique. Differences between the two tumours in vessel size distributions were observed. In CaNT tumours, the proportion of capillary vasculature decreased rapidly with increased tumour size. By comparison, in SaF tumours, the low capillary fraction in small tumours did not change with increasing tumour size.

To determine whether H33342 could be used to investigate regional blood flow changes, the drug pharmacokinetics were investigated. The rate of clearance of H33342 from the blood was very rapid ($T_{\frac{1}{2}} = 110$ s), all visibly detected drug being cleared within 15 min. Vascular volume estimates, obtained following a 1 min exposure to the drug, and values obtained after a prolonged exposure of 15 min, or 15 min followed by a 1 min exposure to a second dose have been compared. Differences in the vascular volume estimates between the groups were both tumour and tumour-size dependent. However, the differences were small, suggesting that neither sluggish flow through some vessels nor transient opening and closing of vessels caused large changes in perfusion over a 15 min period in these tumours.

AN AUTORADIOGRAPHIC APPROACH TO MEASURING REGIONAL BLOOD FLOW IN ANIMAL TUMOURS: PRELIMINARY RESULTS

By G. M. Tozer

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4-iodo [*N*-methyl ^{14}C] antipyrene (^{14}C-IAP) was used as a tracer for blood-flow studies in animal tumours. Antipyrene is an inert, diffusible substance whose distribution within tissues is dependent upon tissue blood flow and the tissue-to-blood partition coefficient. The high spatial resolution of blood flow measurements which can be obtained using this technique makes it particularly suitable for studying the heterogeneous blood supply of tumours.

Quantification of tissue blood flow in ml blood/100 g tissue-min was obtained by the constant infusion of ^{14}C-IAP via the tail vein of rats, carotid arterial blood sampling for ^{14}C activity and the rapid killing of the rat after 30 s to obtain ^{14}C activity in tumour tissue (C_t). Blood flow in each $100\mu m \times 100\mu m \times 20\ \mu m$ tissue volume was measured using scanning densitometry of autoradiographs developed from frozen tissue sections. Computer analysis allowed these results to be displayed pictorially or numerically.

Blood perfusion in grossly necrotic and oedematous regions of a transplanted rat fibrosarcoma, growing in the flank of BD9 rats, was found to be very poor (less than 10 ml blood/100 g tissue-min). Well perfused tumour regions were found lying adjacent to an arterial supply. The uniform perfusion of a spontaneous tubular adenoma growing in the axillary region of a female BD9 rat could be attributed to the tubular arrangement of the tumour, which dictated a regular arrangement of the capillary vasculature. An index of blood flow was used to relate irradiated to unirradiated blood flow in the RIF-1 tumour grown subcutaneously in the flank of C_3H/Km mice. Tumour blood perfusion was found to improve over the first 3 days following a single dose of 20 Gy of X rays.

STUDIES WITH A POTENTIAL ANTI-MELANOMA AGENT: AN α-EMITTING RADIOANALOGUE OF METHYLENE BLUE

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The dye 3,6-(dimethylamino)-phenazothium chloride (methylene blue, MTB) exhibits a high binding affinity for melanin. The β-emitting radioanalogue [^{35}S]-MTB has been shown to cause a significant retardation in the growth of transplanted pigmented melanomas in hamsters but does not affect non-pigmented tumours (Link & Łukiewicz, 1982). A radioanalogue which emits high-LET radiation might prove more efficacious.

The present study concerns such a high-LET radioanalogue, 4-[^{211}At]-MTB. Astatine 211 is a short-lived radiohalogen ($T_{\frac{1}{2}} = 7.2$ h) which decays by the emission of α particles of a mean energy 6.8 MeV, with a mean range in tissue of 60 μm. High-specific-activity preparations of 4-[^{211}At]-MTB have been routinely obtained by thermal heterogeneous isotopic exchange (^{211}At→I) in the presence of 18-crown-6 ether.

An overlap in the distribution of [^{211}At]-MTB and the underlying melanosomes has been demonstrated autoradiographically in the body and dendrites of pigmented B16 melanoma cells grown *in vitro*. No selectivity of uptake was apparent for amelanotic cells.

Preliminary investigations have been carried out with [^{211}At]-MTB and ^{211}At$^-$ on B16 melanoma. Their respective therapeutic efficacies have been determined using the lung colony assay in C57B1/6 mice. Both melanotic and amelanotic melanoma cells were incubated for 1.5 h in medium containing [^{211}At]-MTB or ^{211}At$^-$ (11 kBq/10^5 cells) prior to intravenous injection into mice. Subsequent analysis of the number of melanotic colonies in the lungs of sacrificed mice revealed a significant difference ($p<0.01$) in yield between [^{211}At]-MTB treated and control cells. There was no difference between ^{211}At$^-$ and controls. No therapeutic effect was observed for amelanotic melanoma cells.

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ARE TUMOURS GROWING IN IRRADIATED BEDS MORE HYPOXIC?

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Tumours grow more slowly when implanted into pre-irradiated sites: the tumour bed effect. This effect is thought to be due to the failure of irradiated stroma to form adequate new blood vessels to supply the needs of the growing tumour. Whether such an inadequate vascular supply would result in increased hypoxia has been examined.

An oval portion of flank skin on anaesthetised, C3H/He mice was given 20 Gy X rays as the initial radiation treatment. Twenty-four hours later, 10^5 RIF-1 tumour cells were implanted intradermally into the centre of the irradiated field. Resulting tumours were measured until they reached a volume of 160–200 mm^3. Mice were then given a whole-body dose of 15–25 Gy X rays with tumours either clamped to occlude the blood supply or unclamped. Twenty-four hours later, each tumour was excised and disaggregated and its cells were assayed for clonogenic survival *in vitro*. The hypoxic fraction was calculated from the difference between clonogenic cell survival in the clamped and unclamped tumours.

Two experiments gave the proportion of hypoxic cells as 2.1% or 4.6% for tumours grown in unirradiated beds and 3.7% or 7.1% for tumours implanted into irradiated sites. However, the scatter on the data suggested that this increase in hypoxia was not significant. What was apparent was that, for a given treatment, survival of cells from tumours grown in irradiated beds was more variable than for tumours grown in unirradiated beds.

SITE DIFFERENCES IN THE RADIATION RESPONSE OF RIF TUMOURS IN ANAEMIC MICE

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Iron-deficient anaemia was induced in C$_3$H/Km mice by feeding them a low-iron diet from weaning. These chronically anaemic mice weighed only slightly less than their age-matched controls. However, the haematocrit and haemoglobin levels of the anaemic mice were less than half normal values. RIF tumour cells were implanted either into the gastrocnemius muscle or intradermally in the flank. Tumour radiosensitivity at these sites was measured using *in-vivo* irradiation with an *in-vitro* assay. Intradermal tumours were more radiosensitive in hyperbaric oxygen (HBO) than in air. Tumours implanted in anaemic hosts were more radiosensitive under both air and HBO than those implanted in control animals. However, if the gastrocnemius site was used for implantation then all these differences were radically reduced.

Gut radiosensitivity was assessed using the jejunal crypt survival assay for both chronically anaemic mice and mice made acutely anaemic by venesection 24 h prior to irradiation. Jejunal crypt survival following whole-body irradiation was not influenced by anaemia at doses up to 13 Gy, in either air or 100% oxygen at normal pressure.

Oxygen affinity of haemoglobin, as measured by the level of 2,3-diphosphoglyceric acid, was not altered in anaemic mice, however, blood viscosity was greatly reduced. Therefore, it is suggested that the increase in radiosensitivity in intradermal tumours was due to increased blood flow. Such an increase would be less critical in sites or tissues with a large vascular reserve.

A LYMPH-NODAL TD$_{50}$ ASSAY FOR METASTATIC CELLS

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Experimental studies have been undertaken into the subcutaneous transplantation kinetics of LMC$_1$ rodent tumour cells. These were either prepared as a single-cell suspension or obtained as metastatic cells disseminated spontaneously to, and contained within, lymph nodes removed from primary tumour-bearing rats. For single cell inocula the TD$_{50}$ was about 12 cells (95% fiducial limit 8–20 cells), consistent with the single-cell transplantation kinetics of the LMC$_1$ tumour. For metastatic cells contained within inguinal, axillary and para-aortic lymph nodes the TD$_{50}$ was about 1100 cells (95% fiducial limit 790–1600) but single-cell transplantation kinetics still obtain. Although apparently modified by the trans-lymph-nodal passage of metastatic cells, the incidence and latency of inguinal, axillary and para-aortic metastases in the original, *i.e.* the primary tumour-excised host, were consistent with the TD$_{50}$ data obtained for transplanted lymph nodes.

COMPARATIVE RADIOBIOLOGICAL PROPERTIES OF HUMAN TUMOUR CELL LINES

G. G. Steel, J. M. Deacon, G. M. Duchesne,
L. R. Kelland and J. H. Peacock

*Radiotherapy Research Unit, Institute of Cancer Research,
Sutton, Surrey SM2 5PX*

A published analysis of 51 radiation cell-survival curves determined by various authors on a variety of human cancers (Deacon et al, 1984) has been updated. When divided into five categories, on the basis of clinical radioresponsiveness, values for the surviving fraction at 2 Gy (SF_2) now show a clearer trend. The three most radioresistant categories (Groups C, D, E) have indistinguishable SF_2 values averaging 0.5. Our Group B (small-cell lung carcinoma, medulloblastoma, and perhaps pancreatic carcinoma) average 0.27, Group A (lymphoma, myeloma, and neuroblastoma) average 0.15. The means for Groups A and B were significantly lower than for Groups C, D and E. We, therefore, appear to have identified two categories of human cancer whose cell-survival curves have a steeper initial slope than is found for the majority of human tumours. The implication is that inherent cellular radiosensitivity in these categories is an important determinant of clinical response.

Split-dose recovery has been examined in 14 xenograft types, when the SF_2 value exceeds 0.4 the recovery ratio averages 2.7. Three neuroblastomas whose SF_2 values were close to 0.1 had recovery ratios of about 1.5. Recovery has also been evaluated by measuring the change in radiosensitivity as dose rate was reduced from 150 to 1.6 cGy/min. In seven xenograft lines the low dose rate sparing factor correlates positively with split-dose recovery ratio. There is evidence that the amount of low dose rate sparing slightly exceeds that which would be expected from the size of the β component in fitted linear-quadratic equations.

REFERENCE

DEACON, J., PECKHAM, M. J. & STEEL, G. G., 1984. The radioresponsiveness of human tumours and the initial slope of the cell survival curve. *Radiotherapy and Oncology*, 2, 317–323.

THE RADIATION RESPONSE OF A HUMAN COLON ADENOCARCINOMA GROWN IN MONOLAYER, AS SPHEROIDS AND XENOGRAFTED IN NUDE MICE

C. West

Paterson Laboratories, Manchester

Monolayer cultures of the human colon adenocarcinoma cell line, WiDr, show marked differences in radiation sensitivity with culture age. Maximum and minimum radiation resistance was seen for cells at 2 ($D_0 = 1.7$ Gy, $n = 8$) and 8–12 ($D_0 = 0.9$ Gy, $n = 17$) days after subculture, respectively. Oxygen enhancement ratios were 3.3 for cells irradiated on days 2, 8 and 12. Radiosensitivity did not change when the cells were irradiated either immediately before or after trypsinisation.

A comparison was made of the radiation response of WiDr cells grown in monolayer (Day 5, late exponential), as spheroids (1200 μm in diameter) and as tumours in nude mice (6–8 mm diameter). The radiation response of cell suspensions prepared from tumours irradiated at 4°C in air and tumours irradiated in dead animals was not significantly different from the radiation response of Day 5 monolayer cultures and spheroids irradiated at 4°C, in air and in nitrogen. The estimated hypoxic fractions for tumours irradiated in air-breathing animals and spheroids irradiated at 37°C were 12% and 8%, respectively.

These results showed that the radiation response of WiDr cells grown in monolayer, as spheroids and as tumours in nude mice were very similar, but why late exponentially growing monolayer cultures provide a model for tumour response for these cells remains to be elucidated.

THE EFFECTS OF RADIATION ON MULTICELLULAR SPHEROIDS DERIVED FROM HUMAN TUMOURS OF DIVERSE TYPES

T. E. Wheldon, A. Livingstone, L. Wilson, J. Russell
and J. Adam

*Radiobiology Group, Glasgow Institute of Radiotherapeutics
and Oncology, Belvidere Hospital, Glasgow G31 4PG*

Human tumours differ widely in radioresponsiveness and radiocurability but the mechanisms responsible for this diversity are poorly understood. Though hypoxic resistance has been an important concept, mechanisms based on differences in "intrinsic sensitivity", cellular repair capacity and "contact resistance" are now being considered. Multicellular tumour spheroids (MTS) provide an *in-vitro* model of human cancer which should allow each of these factors to be investigated. Multicellular tumour spheroids have been derived via xenografts from four human tumours of three pathological types: neuroblastoma (two lines), malignant melanoma (one line) and non-small-cell lung cancer (one line). The response to single doses of ^{60}Co radiation was evaluated in terms of specific growth delay and by using a cell-survival estimate based on back-extrapolation of the regrowth curves. These data show wide differences in the radiosensitivity of human MTS, as judged by these criteria. The diversity was sufficiently broad that it could fully account for differences in radioresponsiveness between different tumour types. The two neuroblastoma lines were found to be the most sensitive and the lung cancer line the least sensitive. Considerations of optimal scheduling suggest that the neuroblastoma lines could most effectively be treated using small doses per fraction, if the dose-limiting normal tissues have "late-responding" characteristics. This strategy would be less effective for the other cell lines. *In-vitro* studies using MTS may contribute both to the understanding of diverse clinical responsiveness and to the choice of strategies for improved effectiveness of therapy

BIR Bulletin

January 1987

Quality Assurance Working Party

The working party was set up in 1983 to investigate the ways in which the BIR could contribute to quality assurance work in departments of diagnostic radiology The multidisciplinary membership of the BIR provided people from a wide range of backgrounds, with diverse skills and experience. Over the past three years the membership has changed, but the following people have made significant contributions to the work undertaken· Dr J. H. R Carmichael, Mr M. Fitzgerald, Mr J A. Garrett, Mr D Gifford, Dr P R. R Goddard, Mr W H Grinney, Mrs M. J. Harvey, Mr I R. F Hendra, Mr T. Henshaw, Miss F A Paris, Mr S Stewart and Mr G. Waters.

The main work has been writing a book on quality assurance which would be of value to all the professions with representatives on the working party—not an easy task! However, with much discussion and perseverance a final text has been agreed and it is hoped this publication will be available soon.

The working party also approached the Scientific and Technical Branch of the DHSS NHS Procurement Directorate to request that they include the assessment of diagnostic X-ray quality assurance equipment in their evaluation programme The NHS Procurement Directorate has responded by setting up three quality assurance equipment assessment centres with the enthusiastic collaboration of various establishments in the NHS, as follows: Bristol and Weston Health Authority, Medical Equipment Management Organisation, Horfield Road, Bristol (Mr John Garrett), Regional Department of Medical Physics and Bioengineering, Christie Hospital and Holt Radium Institute, Wilmslow Road, Manchester (Mr John Massey) and St George's Hospital, Department of Medical Physics and Bioengineering, Blackshaw Road, London (Dr John Perry).

The following items are among the initial items to be assessed. Raycheck (Alred Instruments), Hand Held Densitometer (Victoreen), Digital Timer 07-457 (Victoreen), Rad Check with Exposure Meter 06-526 (Victoreen), MINI-X kVp/Time Meter (RTI Instruments) and Model 102 Mammo kVp Cassette (RMI). It is proposed to publish the reports, which will be concise, in a loose-leaf folder to which future reports can be added and old ones subtracted It is expected that the first will be available early this year. Those listed on the mailing list for "Blue Cover" diagnostic X-ray equipment reports will be invited to receive copies Others in the NHS may enrol by contacting Mr C W Hancock, DHSS NHS Procurement Directorate, 14 Russell Square, London WC1B 5EP (Tel 01-636 6822 ext 3206)

Mrs M Jean Harvey, Chairman of the working party, would be pleased to hear from members of suitable areas for consideration by this group or of quality assurance matters which could be addressed by other BIR members

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1987 Nycomed Scandinavian Scholarship Awards

The BIR is delighted to announce that awards of the 1987 Nycomed Scandinavian Scholarships have been made to four BIR members They are Dr A. Adam, Senior Registrar at the Royal Postgraduate Medical School, Hammersmith Hospital, London; Dr J E Gillespie, Consultant Radiologist at Hope Hospital, Manchester, Dr A D. Platts, Senior Registrar at The Royal Free Hospital, London, and Dr D. J West, lecturer at Guy's Medical School, London All the successful applicants are planning to visit Scandinavia in 1987

The Nycomed Scandinavian Scholarship scheme, now in its second year, is generously funded by Nycomed (UK) Ltd (formerly Nyegaard UK Ltd) and administered by the BIR The purpose of the scheme is to enable diagnostic radiologists, usually senior registrars or junior consultants who are interested in diagnostic or interventional intravascular contrast-media procedures, to visit one or more academic departments of radiology in Scandinavia for up to two months of in-depth radiological experience Enquiries about the scheme should be made to Mrs A. Lansdown at the BIR.

Presidential Q.H.P.

Professor R. J Berry, President of the BIR, has been appointed Honorary Physician to Her Majesty the Queen, with effect from January 1, 1987 The appointment is in conjunction with his recent promotion to Surgeon Captain, Royal Naval Reserves, and his forthcoming appointment as Principal Medical Officer (Reserves).

Early days of personal radiation monitoring

My interest has been aroused by the item in the October issue of the *Bulletin* entitled "Monitoring of persons not designated as classified workers". Reference is made to the early days of the personal monitoring service provided by the National Physical Laboratory (NPL) (from November 1942 to December 1955) and by the Radiological Protection Service (RPS) from January 1956 until it was taken over by the National Radiological Protection Board. In view of this reference, the following may be of interest

On the completion of an investigation into photographic measurements of X rays and gamma rays by Dr G. E. Bell we, at the NPL, started to monitor ourselves using dental films Much of our exposure was from radium gamma rays and thus presented no difficulty in regard to dose determination while, in the case of exposure to X rays, the qualities of the radiations used were known and could be taken into account when interpreting the blackening of the films I recollect that Denis Jones also used films for personal dose measurements at the Hammersmith and Lambeth hospitals. At the Royal Cancer Hospital, Mayneord used graphite Sievert chambers, which had the advantage of being quality independent No one, however, regarded the tests as revealing other than what the films and chambers themselves received The devices, being small and located on the body surface, gave no indication of depth dose nor did they give any indication as to the exposure of other parts of the body. Indeed, I can remember when, in November 1942, we offered the service nationally, there soon arose considerable discussion as to whether the film should be worn outside or inside a lead-rubber apron when one was used

The service was introduced at the request of the Ministry of Health because of the concern of Dr A E Barclay (radiological adviser to the Ministry) for the protection of diagnostic radiographers in the EMS hospitals Many of these were being provided with American equipment which had not undergone the careful study that was always given to British equipment before installation Barclay was anxious to avoid a repetition of the events of World War I which led to the setting up of the British X-ray and Radium Protection Committee and ultimately to the International Commission on Radiological Protection We had no choice but to use dental films, knowing full well their unsuitability as a dose-measuring device in the diagnostic X-ray region To overcome this to some extent we calibrated the standard films, against which the test films were compared, using the least radiographically effective quality of radiation likely to be used in a diagnostic department. The result of this was that we overestimated the dose and our reports stated that the dose was "less than" the figure given.

Hospitals were recommended by the Ministry to use the service but it was slow to catch on, the first week's demand amounting to about 40. When the films were returned we had no idea what they would reveal and, to our relief, they indicated a generally satisfactory situation. It had been recommended that the tests should be repeated at quarterly intervals and gradually the demand increased Occasionally, a film was sufficiently blackened to cause some concern, in which case a repeat test was arranged. If it confirmed that the dose could be higher than that recommended, we offered to visit the hospital in order to carry out a survey, the first of which was in May 1943.

Soon after the introduction of the service for diagnostic radiographers it was extended, first to therapy staff and then to industrial workers of all types The same principle of reporting "less than" was adhered to.

I have gone into this amount of detail in order to make clear that the NPL film tests were used essentially as a "tell tale" of working conditions and procedures, and provide no basis upon which to build other than the crudest of personal exposure data. I cannot recollect the threshold dose we adopted, but when it is realised that the "tolerance dose" which at the time could be received "with impunity" was 1 r per week, the figure of (less than) 50 mr does not seem unreasonable.

When the RPS took over the service, the expression "maximum permissible dose" had replaced tolerance dose and its value was less, so it would not be unreasonable if the threshold of reporting had been lowered Moreover, in about 1958, a film badge was introduced which enabled reasonable assessments of the doses received by the films to be made From this time onwards it is possible to utilise the records for cumulative dose estimation but it has to be kept in mind that the errors are considerable In addition to the absence of knowledge of dose distribution and the variability of film as a dose-measuring medium, there is the problem of obliquity. The dose estimations relied on filters of closely controlled thickness and composition and a compromise had to be adopted in the calibration procedure regarding the obliquity of the incident radiation This introduces another source of error.

In all the above circumstances, I consider that the usefulness of any records as a basis of dose/mortality studies for people employed before 1960 is of a highly doubtful nature.

ERIC E. SMITH

Herbert M. Parker: Publications and Other Contributions to Radiological and Health Physics

For more than half a century, Herbert M. Parker was a leading force in radiological physics. As a scientist, he was co-developer of a systematic dosimetry scheme for implant therapy and the proposer of radiological units with unambiguous physical and biological bases. He made seminal contributions to the development of scientifically based radiation protection standards and, as an administrator and manager as well as scientist, helped the Hanford Laboratories to achieve pre-eminence in several areas, including radiation biology, radioactive waste disposal, and environmental radioactivity.

When taken as a whole, Parker's contributions provide an insight into the growth of both medical and health physics Unfortunately, despite their importance, many of Parker's writings are out of print or simply unavailable, as they were never formally published. To make at least his more significant works generally available and to document his accomplishments in the radiological sciences, this volume was compiled by three of his co-workers at the former Hanford Laboratories, where so many of Parker's contributions were made

Published by and available from Battelle Press, 505 King Avenue, Columbus, Ohio 43201, USA (Tel. 614-424 6393), pp 864, 1986, price $55 plus $5 postage (Orders outside the USA require pre-payment in US$ drawn from a US bank with order. air shipment to Europe $31) ISBN 0 935470 36 0.

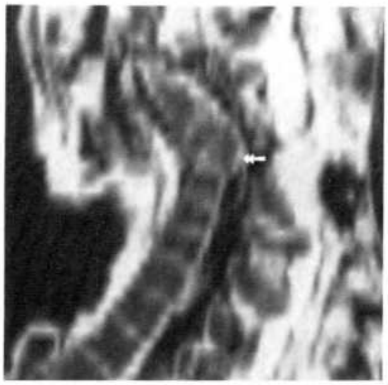
Images of a bog man

Seemingly, the man was stripped, struck twice on the head from behind with an axe-like weapon, received a blow to the back which broke a rib, and, perhaps, was struck in the face, breaking his jaw and splintering a tooth. He was garrotted, alive but unconscious, and then his throat was cut. The bled body was dropped face downwards into a pool in an iron-age bog. And there it lay, in the cold, acidic water, well preserved except for the hands and forearms, until August 1984 when his foot was discovered in a peat-shredding mill. Fortunately, much of the body remained intact; everything below the left anterior superior iliac crest had been taken by peatcutter, but the right lower leg was recovered as a separate item. A flap of leathery skin emerged from the bog, to show where the body was. Pete Marsh, Lindow Man, was with us.

The body has been extensively examined and British Museum Publications has recently produced two books reporting the findings. *The Bog Man,* subtitled *and the archaeology of people,* is a paperback, aimed at the casual enquirer. The other, hardback book, *Lindow Man,* is a collection of fairly detailed academic reports ranging from "Computed tomography of Lindow Man" to "Pollen, charcoal rhizopod and radiometric analyses" to "Boggarts, bogles and Sir Gawain and the Green Knight: Lindow Man and the oral tradition", and has an extensive bibliography. The distinction between the books is to be welcomed, and both books are well written and carry informative and striking illustrations, although the index to the former is regrettably inaccurate. The paperback fulfils its subtitle with a wealth of entertaining anecdotal discussion of preserved bodies in general (including mummies, desiccated Scythians and frozen Greenland Eskimos).

The body underwent an impressive selection of radiological examinations. Plain radiographs were of limited value, as much of the calcium had been leached from the bones by the acidic bog water, giving poor contrast on the films. Xeroradiography at the Royal Marsden was, at first, also disappointing, revealing little more of interest than a depressed coronal fracture fragment. However, the peat then still covering the body and the Delta Lite mount supporting it were responsible for this. After they had been removed, a subsequent series was taken. These demonstrated a large bone fragment driven inside the skull by the blows to the back of the head, as well as a long crack at the back of the skull, the broken rib and a broken vertebra, all caused by blunt weapons. Xeroradiographs of the thorax revealed both clavicles, the sternal ends of which were indistinct and barely distinguishable, suggesting partial or recent fusion, thereby giving an estimate of the age of Lindow Man (from Krogman's ages for the fusion of the ossification) of 25–28 years.

Computed tomography provided more information than the other radiological techniques. A General Electric 9800 scanner at the Middlesex Hospital was one of the few scanners available with a large enough aperture to take the body in its unconventional position. One hundred scans were taken in two hours, the body being repeatedly sprayed with water to keep it cool and damp. The decalcification was evident: attenuation values in Lindow Man ranged from −267 to −650 HU. Internal organs were not identified, although there was amorphous soft tissue in the cranium, symmetrical about the midline and surrounded by air on the right and left, suggesting brain tissue. The eyes could not be identified. Also, within the spinal canal of many of the vertebrae a thin sheet of soft tissue with a triangular configuration appeared to be the remains of dura mater. Reformatting the axial images into the longitudinal projection revealed a very sharp angular deformity at the junction of the third and fourth vertebrae, corresponding exactly with the superficial site of the garrotte.



Longitudinal reconstruction of cervical spine showing angular deformity between third and fourth cervical vertebrae. Taken by Miss Marion Hallet, Superintendent Radiographer at St Bartholomew's and reproduced from *Lindow Man* with kind permission of British Museum Publications.

Picker International Ltd performed the magnetic resonance imaging. The intracranial contents were again seen, as well as arthritic degenerative changes in the spine, Schmorl's nodes, also imaged by CT.

The non-invasive imaging played an important part in the planning of the autopsy. In fact, because the lower trunk had been cut, the inside of the torso could be investigated without any incisions being made. The anterior and posterior walls of the abdomen could be parted easily; much of the tissue had decayed, but the stomach, duodenum and jejunum had remained and still contained partly digested food. Endoscopy via the throat came to an abrupt halt at the level of the break in the neck. The constriction, it was judged, would have prevented the passage of water into the alimentary tract. This allowed a detailed study of Lindow Man's last supper. Electron spin resonance was able to demonstrate that the wheat chaff found was eaten as bread, cooked at about 250°C, rather than porridge, which would have been cooked at nearer to 100°C.

Lindow Man is now on display in the British Museum until February, after which the exhibition will travel to other cities in the UK. *Lindow Man, ed. by I. M. Stead, J. B. Bourke and D. Brothwell, pp. 208, 1986, £15.00, ISBN 0-7141-1386-7, and the Bog Man and the archaeology of people, by D. Brothwell, pp. 128, 1986, £5.95, ISBN 0-7141-1384-0, are both published by British Museum Publications Ltd, London.*

R. J. Footring

Journal of Interventional Radiology

Churchill Livingstone have recently launched this new journal to cater for the specialty. It is intended to be an international forum for clinicians involved in interventional procedures, with emphasis on the practical aspects, such as equipment and techniques. The subjects covered by the journal include all interventional procedures conducted under imaging guidance and the relevant imaging techniques, as well as the organisational and administrative aspects. The journal has an international editorial board chaired by Dr D. J. Allison.

ISSN 0268-0890, Vol. 2 £45 (individual rate), £60 (institutional rate), four issues (Churchill Livingstone, Edinburgh).

To our US readers

BJR supplements now available from MPPC

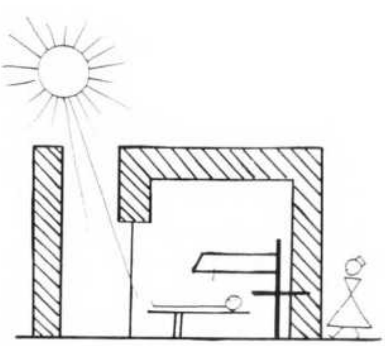
John Cameron, Emeritus Professor of Radiology at the University of California, has recently set up his own organisation, the Medical Physics Publishing Corporation, for the purpose of publicising and distributing radiological—especially physics-orientated—literature in North America. The Institute has granted MPPC the right to sell its publications (excluding the *BJR*) and these are now available *direct* from MPPC, 118 N Breese Terrace, Madison, Wisconsin 53705 (Tel. 608-238 3223) at the following rates.

Supplement No. 16	$10
Supplement No. 17	$17
Supplement No. 18	$29
Supplement No. 19	$32
Basic Clinical Ultrasound	$23.

(Full catalogue also available from MPPC upon request.)

Daylight access to radiotherapy treatment rooms

The new radiotherapy extension to the Kantonsspital Aarau, Switzerland, incorporates two supervoltage treatment rooms of a novel design. The aim was to have full daylight access to the rooms, so that they would provide a more attractive environment for patients and staff. This was achieved by a "vertical maze" type of construction, as shown in the diagram, which made possible windows along the complete length of one wall of the room (see photograph).



New radiotherapy extension to the Kantonsspital.

Radiation accidents due to software faults

Reports in the *New York Times* and the *Boston Globe* last June suggest that software faults could have caused three radiation overtreatments using Therac 25 machines. It seemed that "if an extremely fast-typing operator inadvertently selected the X-ray mode, then used an editing key to correct the command and select the electron mode instead, it was possible for the computer to lag behind the orders. The result was that the device appeared to have made the correct adjustment but in fact had an improper setting so it focussed electrons at full power to a tiny spot on the body." The computer screen did not give a correct indication of what was going on. The software fault has since been corrected by the manufacturers.

Press releases

Doppler echocardiography can be quantified

The cardiological evaluation system CARDIO 200 is now equipped with a program for evaluating cardiological Doppler echoes. By simply tracing the diastolic/systolic spectral curves on the recording paper or on-line from the image on the monitor, the user obtains the Doppler-related parameters such as velocity, pressure, valve opening area, different time intervals, regurgitation, cardiac output, etc. The patient's data, the diagnosis text, the curves traced and all other data can be printed out or stored and statistically evaluated.

Thus, CARDIO 200 allows the user to perform many and various evaluations of the M-Mode, Sector and Doppler echoes, cinefilm, catheter and His-Bundle examinations together with statistical evaluations.

For further details: International Marketing Services, Kontron S.p.A., Via G. Fantoli, 16/15–20138 milan, Italy.

New pocket radiation alarm

The "Monitor Personal Alarm" made by Collingwood Electronics is worn like a radio-pager and is pre-set by the user to one of three radiation values ranging from 0.25 mR/h to 2.50 mR/h. Radiation received by the integral miniature Geiger-Müller tube triggers solid-state circuitry to produce a repeated visual and audible warning.

The dose-rate range for the unit is 0.004–3000 mGy/h and the energy range is 30 keV to 1.25 MeV. Battery life is around 5000 h and the unit measures 97 mm × 42 mm × 14 mm. Weighing 60 g, the monitor is fully enclosed in an ABS casing, with a clip for pocket or belt wear. Operating temperature is from −10°C to +50°C, and the unit is priced at £139.50.

For further information please contact: Richard Atkins, Collingwood Electronics, 48 Collingwood Road, Great Yarmouth, Norfolk NR30 4LR (Tel. 0379-52336 or 0493-842022).

Future annual meetings on magnetic resonance in medicine

The increasing number of medical conferences in all disciplines has not led to a higher quality of scientific presentations. Thus, the choice of which meeting to attend has grown more and more difficult for participants, speakers, and commercial exhibitors, and the same papers are often presented at several meetings.

To prevent such an undesirable development in their field, the European Society of Magnetic Resonance in Medicine and Biology and the European Workshop on Nuclear Magnetic Resonance in Medicine have decided to organise joint annual meetings. The first one will be held at University College, London, from March 25–27, 1987. This conference will be in co-operation with the European Federation of Organisations for Medical Physics. The 1988 meeting will take place in the Federal Republic of Germany.

The goal of this co-operation is to create a common European platform for both continuing education and scientific exchange between the European research groups.

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085)

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Practical Aspects of Magnetic Resonance Imaging
January 14, 1987 at 9 30 a m
Middlesex Hospital Medical School, London
Chairman: Professor I Isherwood
Speakers Dr M. Smith, Dr G Bydder, Dr B. Kendall, Professor I Isherwood, Dr J P. R Jenkins, Professor B Worthington and Professor J. J K Best.
Joint BIR/RCR meeting

Uroradiology Update
January 15, 1987 at 5 30 p.m
Chairman: Dr D. Rickards. Speakers. Dr D Rickards, Dr J Pemberton, Dr C. E. L. Freer, Mr G. Watson, Dr R. Johnson, Dr W. Lees, Professor D J Allison
Joint BIR/RCR/RSM meeting

Radionuclide Investigations of the Lung
February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting
February 13, 1987 at 9 30 a m
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems
February 25, 1987 at 9 45 a m
Middlesex Hospital Medical School, London
Chairman. Professor I Isherwood
Speakers. Dr O. Craig, Mr D. Rothery, Dr C Taylor, Dr W. Lees, Mrs J E Burnett, Dr R. Rupprecht, Professor L Gillanders, Mr H. Griffith, Mr P. Vernon, Mr C Robertson, Mr J Tiemann and Dr C Greinacher.
Topics will include image display, image transmission and image storage
All day meeting organised by Industry Committee

Annual General Meeting
May 14, 1987 at 4 30 p m

Imaging in Radiotherapy
May 15, 1987
Chairmen. Dr D Thwaites and another to be announced.
Joint IPSM/BIR all day meeting organised by IPSM

Dysphagia and Disorders of Swallowing
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM

Conversazione
May 20, 1987
Royal Naval College, Greenwich

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1-3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include
The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"
The BIR Mayneord Lecture (sponsored by 3M UK plc), by Dr Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"
The RCR George Simon Lecture, by Dr J C. Batten, "Radiology and cystic fibrosis"
The BIR Presidential Address, by Professor R J. Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

For further information and registration forms please apply to the Assistant Secretary Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085)

Patrick Grove Memorial Fellowship

The Radiological Research Trust was very pleased indeed at the number and quality of applications for this fellowship, generously funded by Amersham International

The first Fellow was appointed on November 18, 1986. Dr Adnan P Richardson of the Kent and Canterbury Hospital Nuclear Medicine Department will receive about £20 000 per annum in salary and expenses for three years to pursue his study of site-specific labelling of antibodies for radioimmunolocalisation of tumours The thrust of the work will be towards the chemistry of labelling and, if the originality of the idea bears fruit, may have wide applications.

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a m.–5 p.m., and Thursdays 11 a.m.–7 p.m, and Mrs Angela Lansdown, daily 9 a.m.–5 p m. (Tel. 01-580 4085)

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Bassett, L W, Gold, R H. & Kimme-Smith, C.: Hand-held and automated breast ultrasound 1986
ICRU Report 38: Dose and volume specification for reporting intracavitary therapy in gynecology. 1985
Jeanmart, L (Ed.): Tumors (radiology of the spine) 1986
NCRP Proceedings No. 6: Some issues important in developing basic radiation protection recommendations. Ed by T M. Koval 1985
NCRP Report No. 75: Iodine 129. Evaluation of releases from nuclear power generation 1983
Patel, P R: Multiple choice questions in radiology 1986
Reeder, M M & Palmer, P E S.: Radiology of tropical diseases 1981

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor

Courses in Abdominal and Obstetrical Ultrasound
Basic Practicum
January 12–16, May 11–15, November 16–20, 1987
Advanced Obstetrics and Gynecology
April 8–10, 1987
Advanced Practicum in Ultrasound
December 7–11, 1987
Visiting Physicians
Year round, by appointment only
Baltimore, Maryland, USA
Further details. Joan Moemiller, Department of Radiology, Johns Hopkins Hospital, Baltimore, Maryland 21205, USA (Tel 301-955 8450)

Intensive Nuclear Medicine Course for F.R.C.R. Students
January 30–31, 1987
St Thomas' Hospital, London
Cost of course £45
Further details and application form: Miss Erica Mendy, Postgraduate Centre, St Thomas' Hospital, Lambeth Palace Road, London SE1 7EH (Tel. 01-928 9292 ext 2072)

Advanced Course in Diagnostic Imaging
February 8–13, 1987
Singapore
Further details. Professor Lenny Tan, Academy of Medicine, PO Box 694, Tiong Bahru Post Office, Singapore 9116, Republic of Singapore.

The Bart's MCQ Course
February 21, 1987
St Bartholomew's Hospital, London
Further details. Miss V. Francis, MCQ Course Secretary, St Bartholomew's Hospital, X-ray Department, 4th Floor OPD, West Smithfield, London EC1A 7BE (Tel. 01-601 8303).

Positron Emission Tomography and the Chemistry of Mental Illness
March 12–13, 1987
Baltimore, Maryland
Further details: Pamela E. Macedonia, Program Coordinator, Turner 22, 720 Rutland Avenue, Baltimore, Maryland 21205, USA (Tel. 301-955 6085).

London Course in Whole Body Computed Tomography
March 15–19, 1987
Gleneagles Hotel, Auchterarder, Scotland
Further details: Mrs J O'Donnell, Organising Secretary, Department of Radiology, Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT.

Ultrasound Update
March 18, 1987
Hillingdon Hospital, Uxbridge
Course organiser. Dr Diz Shirley
Further details: Postgraduate Administrator, Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN (Tel 0895-37964 or 38282 ext 253).

Tutorials in Laser Angioplasty and Interventional Radiology
March 30–April 1, 1987
Baltimore, Maryland, USA
Further details: Program Co-ordinator, Office of Continuing Education, The Johns Hopkins Medical Institutions, Room 19 Turner, 720 Rutland Avenue, Baltimore, Maryland 21205, USA (Tel. 301-955 3168).

Annual London Spring Seminar in Medical Diagnostic Imaging
May 2–10, 1987
London
Further details Spring Seminar, 21915 Roscoe Blvd, Suite 222, Canoga Park, CA 91304, USA (Tel. 818-340 0580, ext 280)

5th International Nijmegen Vascular Symposium: angioplasty, vascular surgery, combined approach
May 15–16, 1987
Nijmegen, The Netherlands
Further details Dr S H Skotnicki, University Hospital St Radboud, 6500 HB Nijmegen, The Netherlands.

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details: Secretariat ECR '87, SPRMN, Av Elias Garcia, 123–7° DTo, 1000 Lisboa, Portugal, (Tel 77–05 30, Telex 62074 SPRMN P).

Radiology of the Small Intestine
June 12, 1987
John Radcliffe Hospital, Oxford
Further details. Dr D. J Nolan, Dept of Radiology, John Radcliffe Hospital, Oxford OX3 9DU (Tel. 0865-817 238).

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel 01-935 5726, ext 206).

International Symposium on Dosimetry in Radiotherapy
August 31–September 4, 1987
Vienna, Austria
Further details Secretariat IAEA-SM-298, c/o International Atomic Energy Agency, PO Box 100, A-1400 Vienna, Austria (Telex No 1-12645. Cable address INATOM VIENNA)

Intra-operative Ultrasonography
September 18–19, 1987
Paris, France
Further details Convergences, 16 rue Jean Jacques Rousseau, 75001 Paris, France.

5th Asian-Oceanian Congress of Radiology
September 21–25, 1987
Seoul, Korea
Further details Man Chung Han, M.D., Secretary General, 5th Asian-Oceanian Congress of Radiology, c/o Department of Diagnostic Radiology, Seoul National University Hospital, 28 Yunkun-dong, Chongro-ku, K P.O. Box 1880, Seoul 110, Korea

Automation Means in Preventive Medicine '87
September 28–October 2, 1987
Pestany, Czechoslovakia
Further details. The Industry and Technology Division, United Nations Economic Commission for Europe, Palais des Nations, CH-1211 Geneva 10, Switzerland.

4th International Symposium on Audiological Medicine
November 8–11, 1987
Tenerife, Canary Islands
Further details Dr Jose Barajas, Perez de Rozas 8, 38004 Santa Cruz de Tenerife, Spain

7th International Congress of the International Radiation Protection Association: radiation protection practice
April 10–17, 1988
Sydney, Australia
Further details IRPA 7 Secretariat, GPO Box 2609, Sydney, NSW 2001, Australia (Tel 02-241 1478, Telex AA74845 "Consec", Cable "Convention" Sydney).

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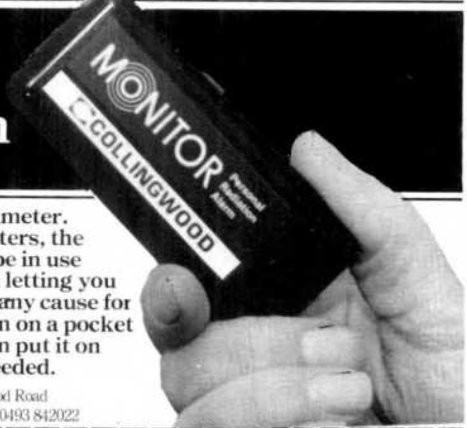

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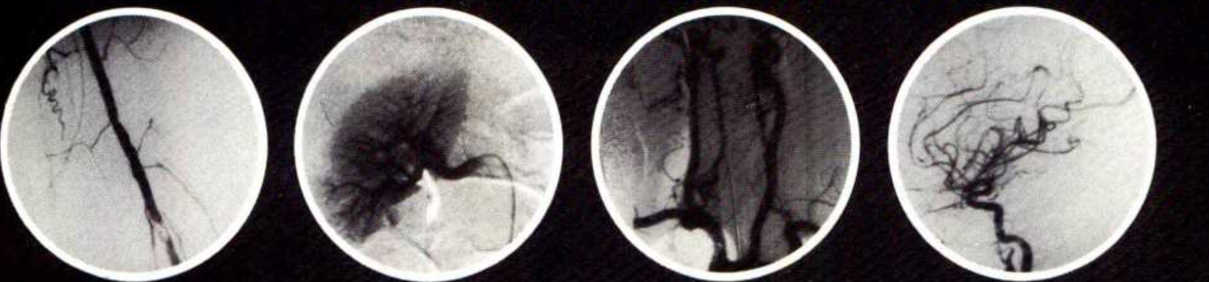

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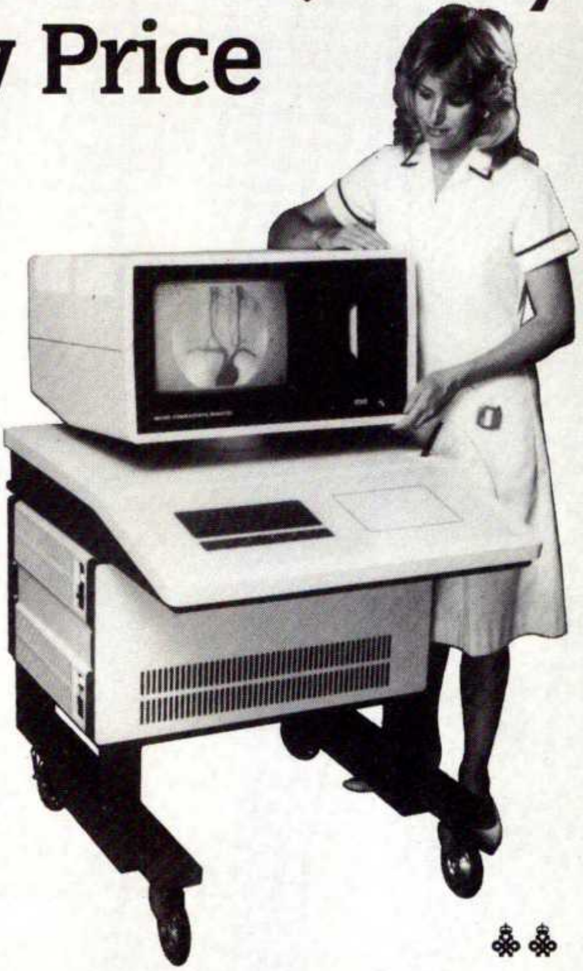

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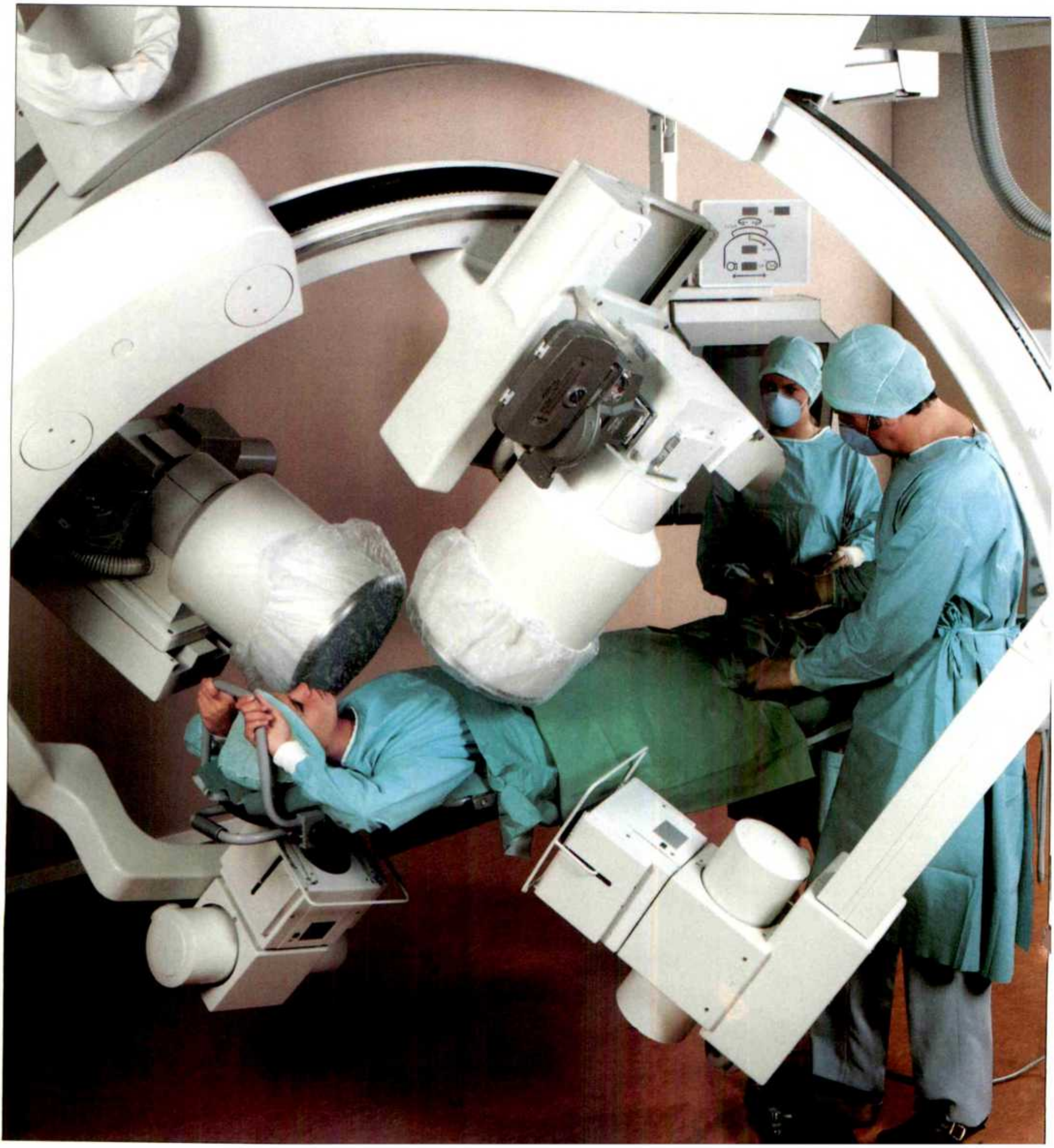

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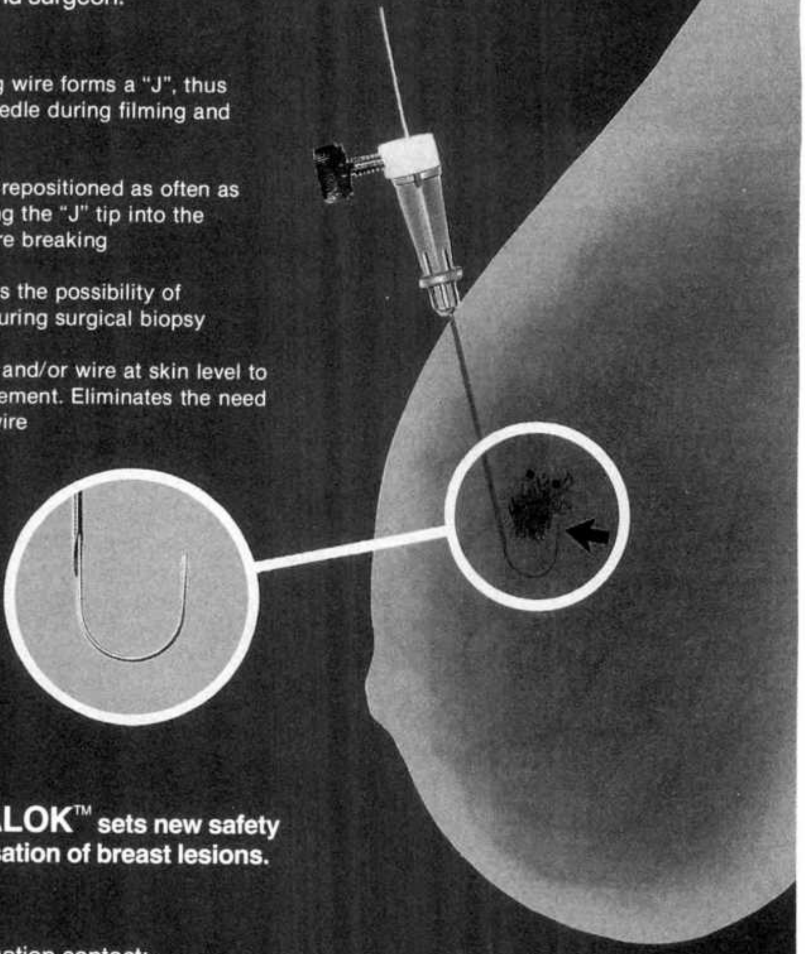

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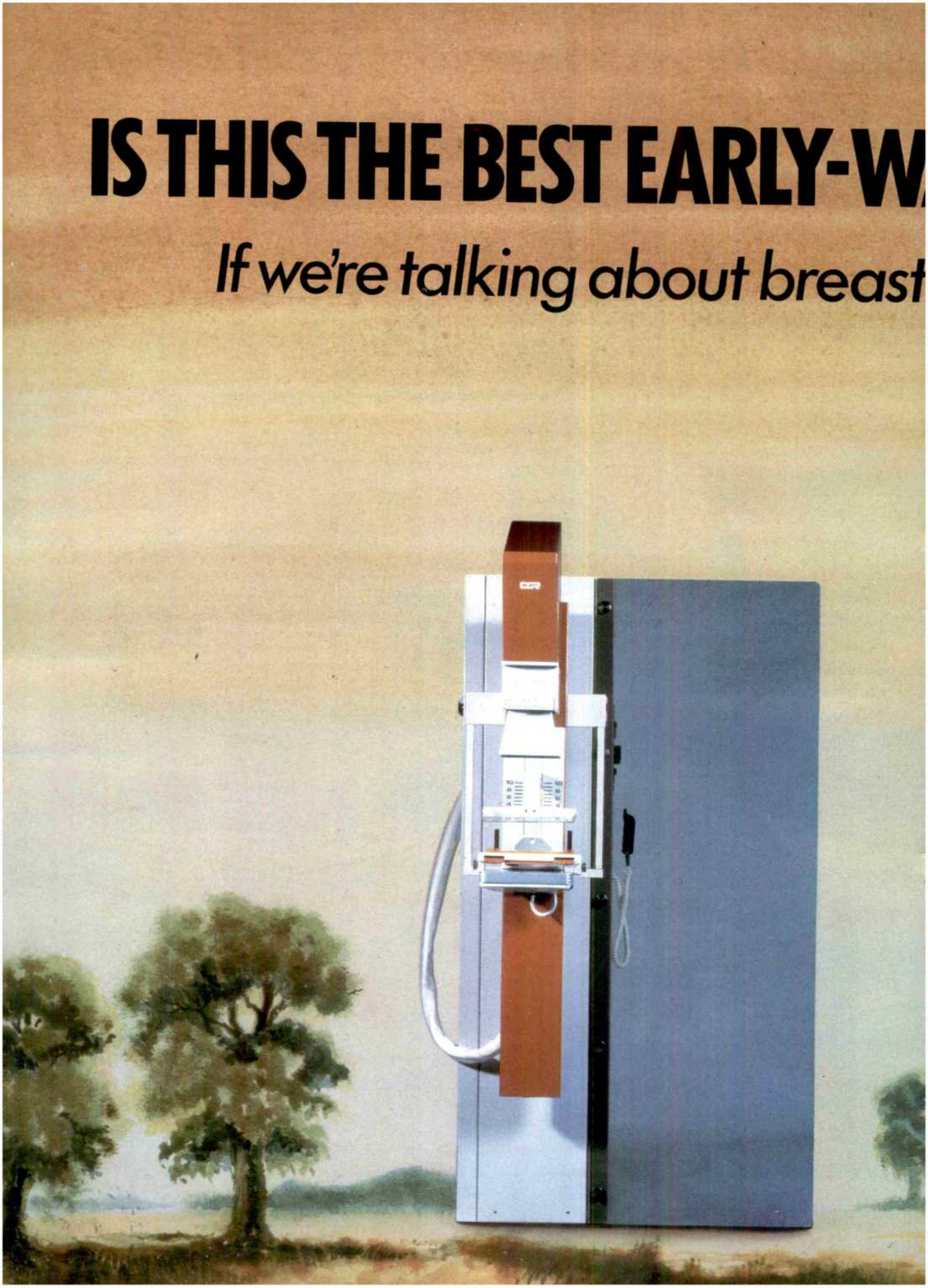

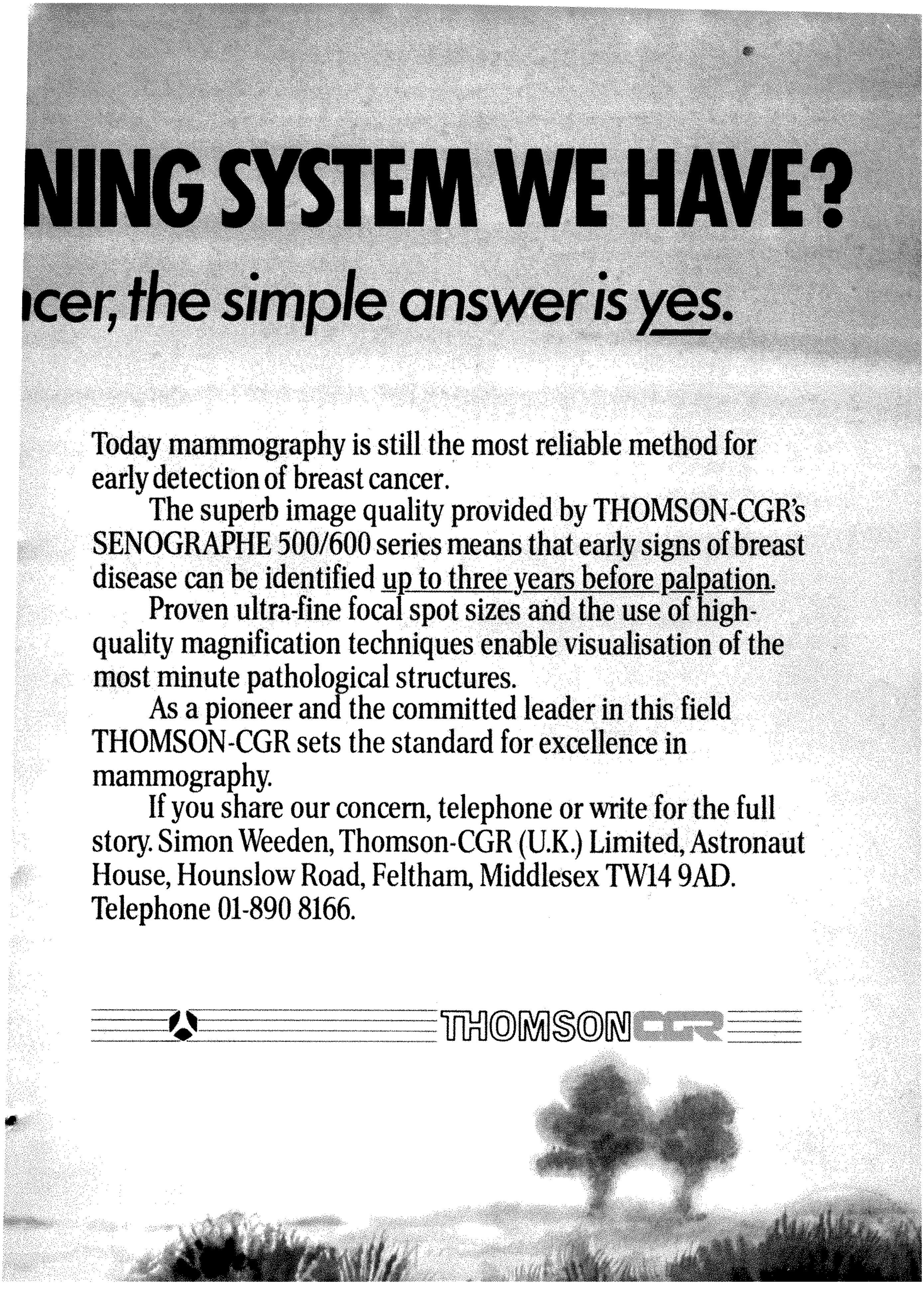

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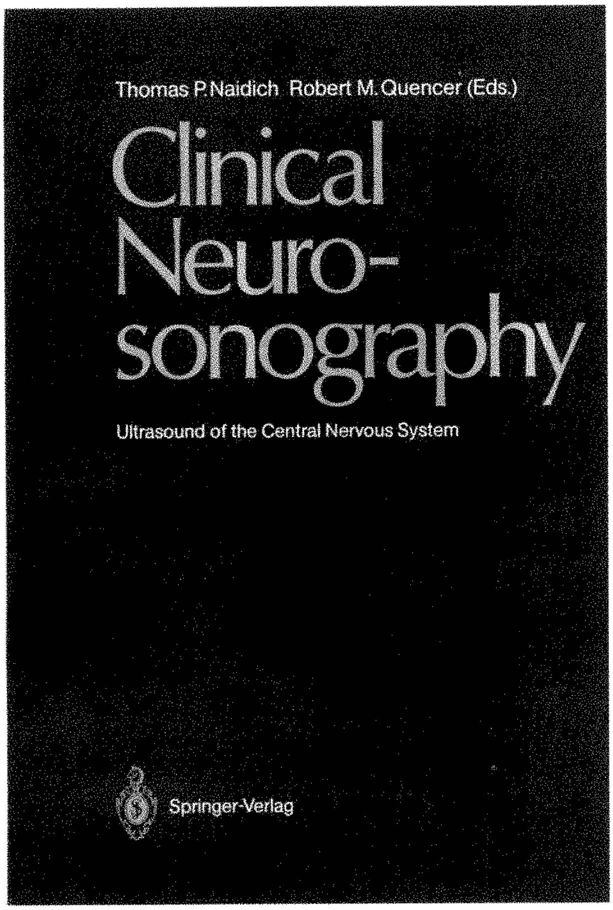
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The autors of this book have reviewed neurosonography in separate sections on fetal neurosonography, the neonate head, the neonatal spine, intraoperative neurosonography, post-operative neurosonography, carotid sonography, and orbital echography. In each section, these authorities discuss basic diagnosis, present recent advances in the area, and provide new information not available elsewhere.

A. Valavanis, O. Schubiger, Zürich; **T. P. Naidich,** Chicago

Clinical Imaging of the Cerebello-Pontine Angle

1986. 138 figures. Approx. 205 pages.
Hard cover DM 198,–. ISBN 3-540-16553-3

This book describes the diagnostic problems encountered in cerebellopontine angle lesions. Special attention is directed to the differential diagnostic criteria for each specific lesion. It is the authors' aim to help the reader arrive at a precise, if at all possible, histologic diagnosis.
The former radiological methods of examination are briefly reviewed, but the main stress is on computer tomography. The reader can learn how to overcome technical imperfections inherent in all CT equipment. A special chapter is devoted to the present state-of-the-art of magnetic resonance imaging.
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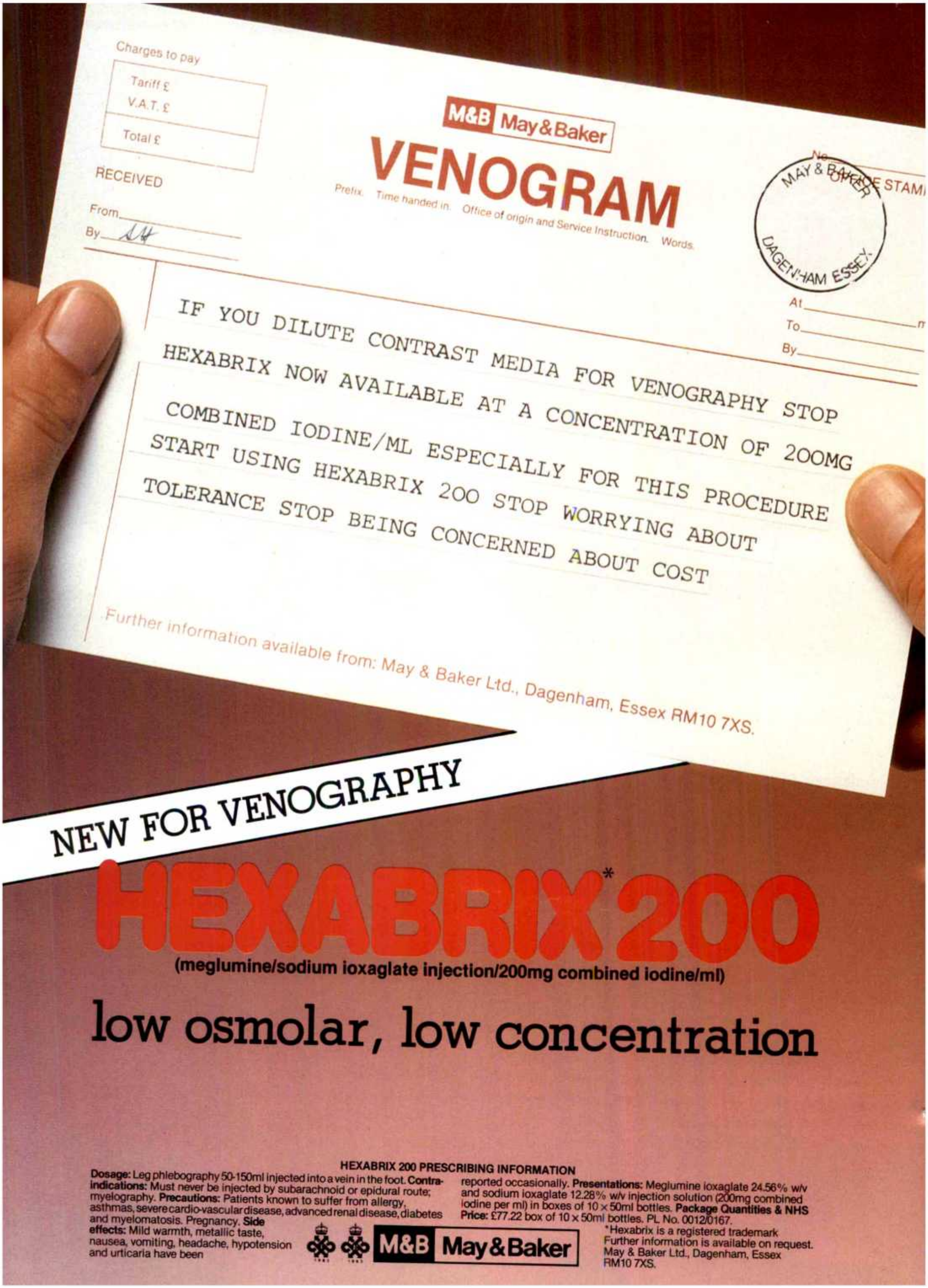

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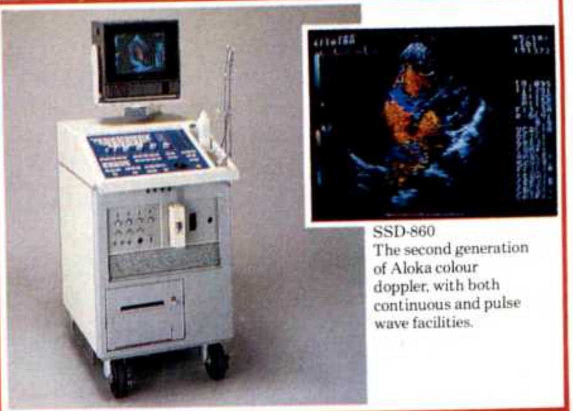

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Colour display of quantitative blood flow and cardiac anatomy in a single magnetic resonance cine loop

By R. H Klipstein, B.A., M.B., B.S., D. N. Firmin, B.Sc., M.Phil., S. R. Underwood, M.A., B.M., M.R.C.P., *G. L. Nayler, B.A., R. S. O. Rees, M.A., F.R.C.P., F.R.C.R. and D. B. Longmore, F.R.C.S.

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ABSTRACT

A method of displaying on a single image both the anatomical and the quantitative blood-flow information obtainable from cardiac magnetic resonance has been developed. Anatomical and parametric blood velocity images are combined to produce a computer-processed composite image suitable for display with a specially designed colour scale Methods for dealing with imperfections in the input images and for obviating technical problems encountered in computer cine display are described The clinical application of the method is illustrated using eight coronal frames from a normal subject

Since the development of methods of gating the acquisition of magnetic resonance images of the heart (Steiner et al, 1983), progress has been rapid. Detailed anatomical (Hawkes et al, 1981; Nishikawa et al, 1983; Higgins et al, 1984; Higgins et al, 1985b) and pathological (Steiner, 1984; Zeitler & Schurerer, 1984; Higgins et al, 1985a) information is available. Cine acquisition (Waterton et al, 1985) allows the details of contraction to be studied. Parameters of cardiac function may be derived Chamber volumes, stroke volumes, ejection fractions (Longmore et al, 1985), regional wall motion (Rees et al, 1985; Underwood et al, 1986) and ventricular wall thicknesses (Fisher et al, 1985; Underwood et al, 1986) can be measured with considerable accuracy.

Complementary information on cardiac function is available from blood-flow measurement. A variety of magnetic resonance methods for measuring blood flow exists (Moran, 1982; Singer & Crooks, 1983; van Dijk, 1984; Bryant et al, 1984; Axel, 1984; Wedeen et al, 1985a,b). Some are semiquantitative and others quantitative. The method of phase-mapping (Bryant et al, 1984) used in our department accurately measures the component of blood velocity in a defined direction so that velocity profiles of blood flow in the heart and blood vessels may be obtained.

Enhancement of information on cardiac function may be achieved by cine display of frames taken at various points in the cardiac cycle (Minato et al, 1982). In the case of magnetic resonance, this may be done for either anatomy or flow, but there would be greater enhancement from displaying both types of information on a single image, and presenting a series of such images as a cine loop. This paper describes a display method which achieves this using magnetic resonance data.

INSTRUMENTATION

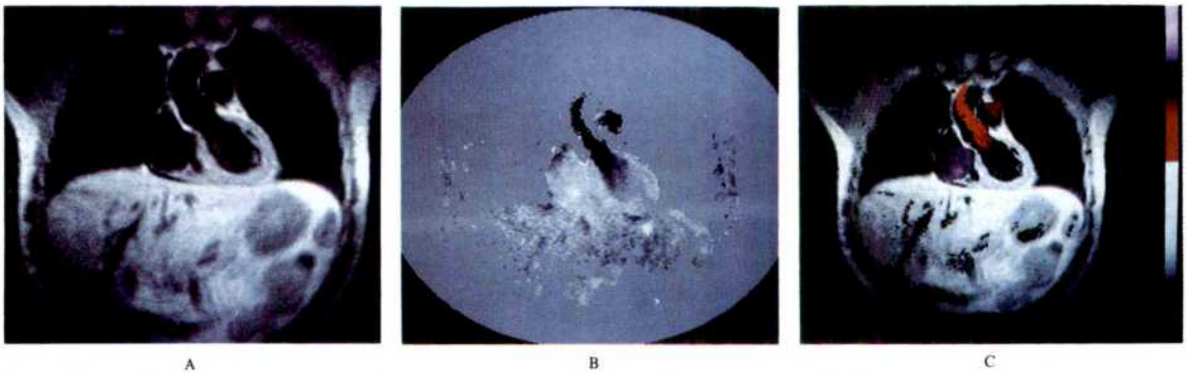
Both the anatomical and the flow images were obtained on a Picker International Vista MR 2055 magnetic resonance scanner operating at 0.495 T. The details of acquisition and processing of both the anatomical and the flow images have been described elsewhere (Steiner et al, 1983; Bryant et al, 1984). Data acquisition for the flow images takes roughly 10 min for 12 cine frames, the precise time depending on heart rate.

After acquisition, the images were copied to a Sperry-Univac V77-600 computer system for off-line processing. This system is equipped with a colour display monitor. The viewing software is supplied for nuclear medicine systems by Nodecrest Ltd and it has facilities for design of colour scales. The image processing programs have been written in this department in FORTRAN and in assembly language by one of the authors (R.H.K.).

METHODS

The anatomical image is a matrix of 256 × 256 pixels in the range 0 to m. The value of m is varied with the magnetic resonance sequence used, but typically it is of the order of 1500 for the spin-echo sequence most commonly used for cardiac images (TE = 24 ms).

The flow image is also 256 × 256 pixels with values in the range $\pm n$. The value of n varies with the range of velocities to be covered, but it is usually set to a maximum value of the order of 1000. In this study the maximum velocity was 1 m/s, so that the pixels effectively calibrated flow in mm/s.



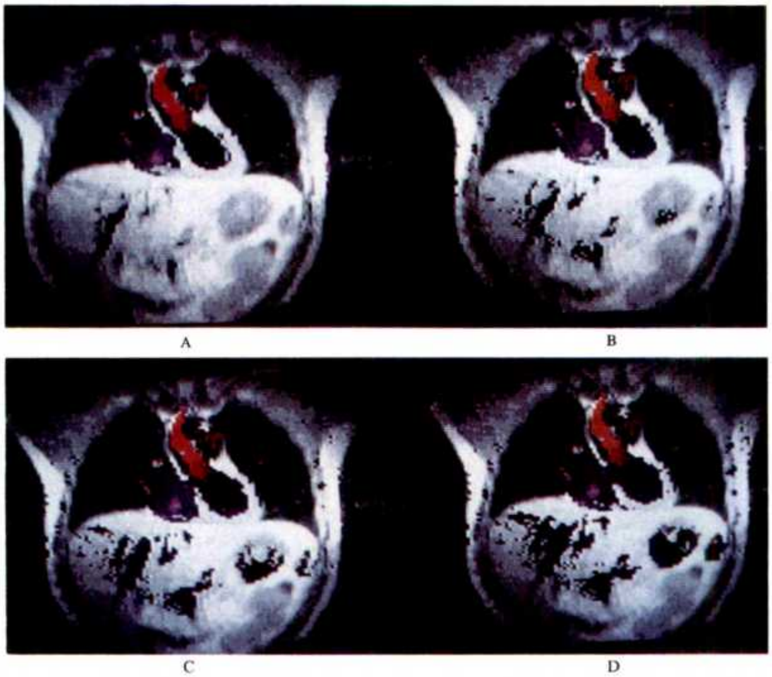


FIG. 2.

The effect of differing anatomical image thresholds. Those used here are (A) 20%, (B) 25%, (C) 30% and (D) 35% of the maximum anatomical image pixel value, *m*. As the threshold is made higher, less of the flow information is ignored, allowing areas of very low flow to encroach on the anatomical information. In this series this is seen below the diaphragm and in the progressive disappearance of the superior part of the left ventricular septum from (B) to (D). The flow noise threshold for this series was 1%.

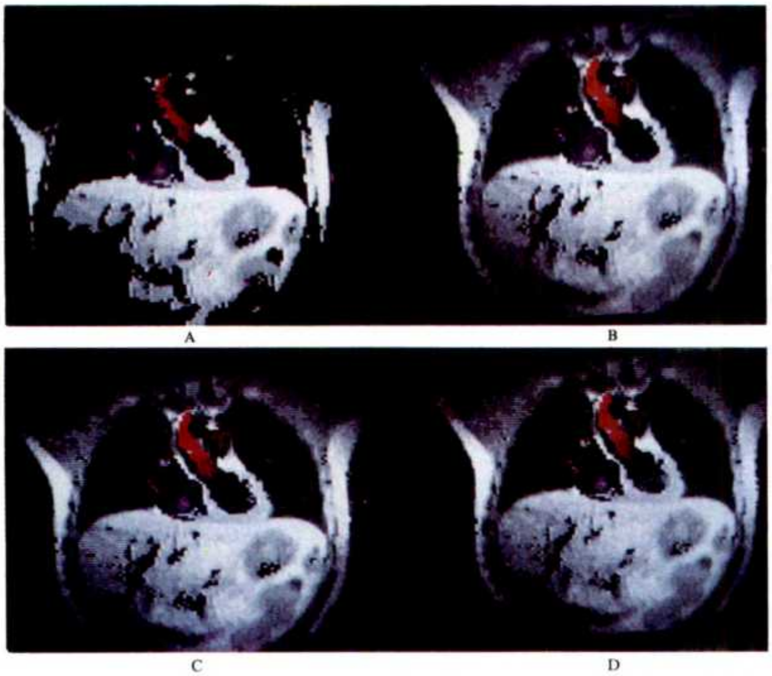


FIG. 3.

The effect of differing flow noise thresholds. Those displayed are (A) no thresholding, (B) 1%, (C) 2% and (D) 5% of the maximum flow image pixel value, *n*. This threshold is only critical at the low end of the range, as shown by the difference between (A) and (B). As this threshold is raised, the outer envelope of the flow information moves into the lumen of the chamber or vessel (D). The anatomical image threshold was 25%.

Blood flow and cardiac anatomy in colour on MRI

FIG. 1. *(left)*

An anatomical image (A), a phase map depicting blood flow in the head–foot direction (B) and combination to form the composite image (C). Note the dark lumina of the chambers and vessels in (A) into which the flow map of (B) will fit. The flow map encodes blood flow towards the head in black, towards the feet in white, and zero flow in mid-grey, the highest velocities shown being 1 m/s. The flow information is transferred into the composite image with flow towards the head in red and towards the feet in purple. The composite image colour scale is displayed on the right of (C).

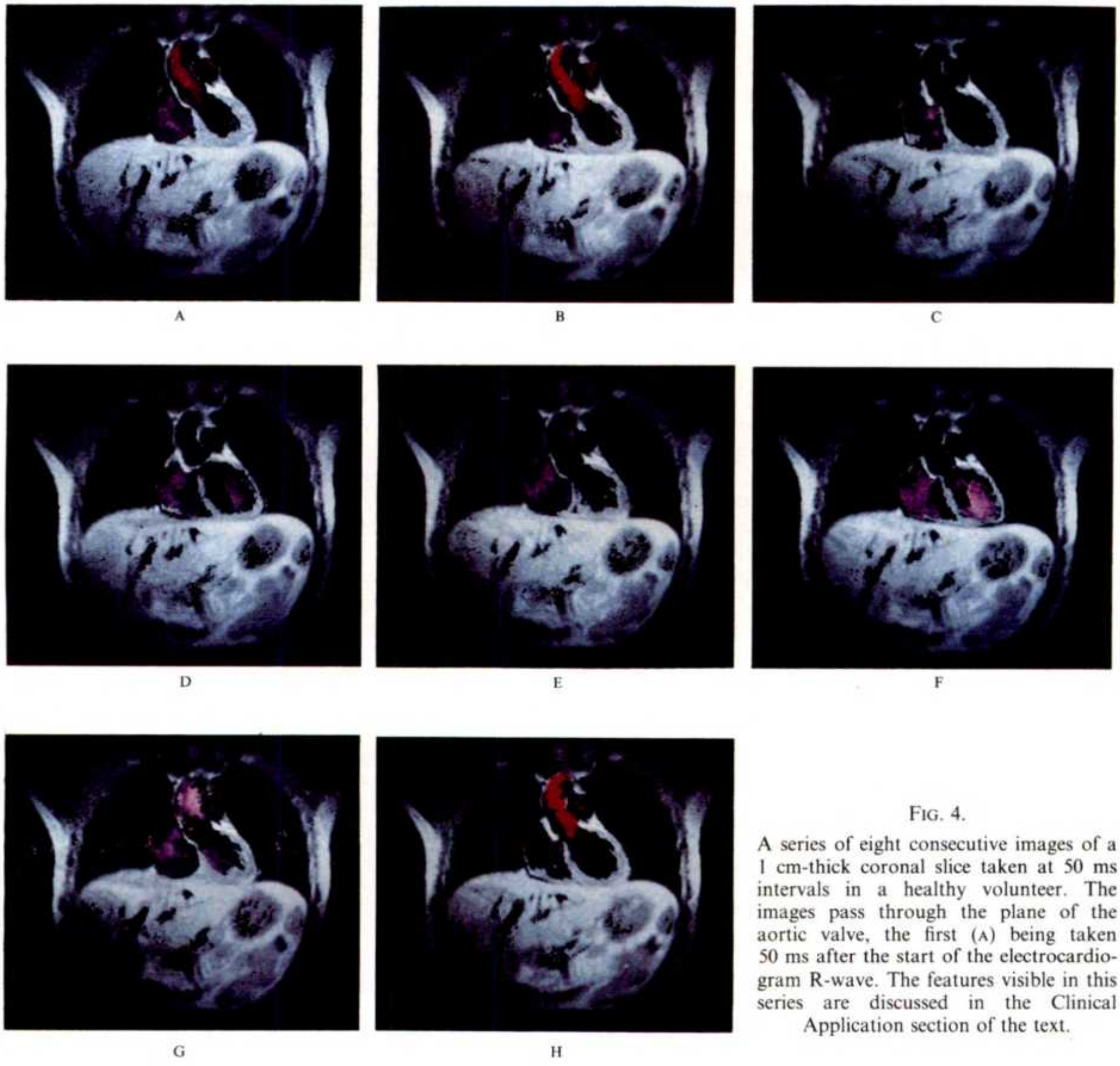


FIG. 4.

A series of eight consecutive images of a 1 cm-thick coronal slice taken at 50 ms intervals in a healthy volunteer. The images pass through the plane of the aortic valve, the first (A) being taken 50 ms after the start of the electrocardiogram R-wave. The features visible in this series are discussed in the Clinical Application section of the text.

The flow image is parametric, its values being directly proportional to the component of velocity in a defined direction. This direction may lie within the image plane, running horizontally or vertically, or it may be perpendicular to the image plane. Positive pixel values signify flow in the forward direction; negative values in the reverse.

These two images are mapped point by point on to a third image (the composite image). The values of the anatomical and flow images for each point are examined and a decision made as to which should be used. This is possible because spin-echo sequences (Hahn, 1950) give very little signal from flowing blood (von Schulthess et al, 1985), but flow images show mainly flowing blood in the vessels

The decision on whether to use the information from the anatomical or the flow image is not as simple as taking the pixel with the higher value Two sources of error complicate the decision, namely motion artefact (Schultz et al, 1984) and signal from very slowly moving blood at end-diastole (von Schulthess et al, 1985), necessitating the use of two additional criteria. The first depends on the fact that a high anatomical pixel value must arise from a structure other than blood in a vessel. The second exploits the fact that (following a type of thresholding intrinsic to the processing of the flow image) pixels in this image which have very low values are likely to be noise. Thus, if the anatomical image pixel has a value larger than a pre-set fraction of m (the anatomical image threshold), or the absolute flow pixel value is below a selected threshold (the flow noise threshold), the anatomical image pixel is to be used.

Grey-scale transformations (Rosenfeld & Kak, 1982a) are employed so that pixels coming from the anatomical image are in one range and those from the flow image in another. The two ranges are displayed with anatomy in black and white and flow in colour. The choice of colour is arbitrary, provided that the forward and reverse directions of flow are displayed in colours perceived by the human eye as independent. In our study red and purple were used.

The colour scale is, thus, in three parts, namely a grey scale, a scale of uniformly descending brightnesses of red and a scale of uniformly ascending brightnesses of purple. Sixty-four levels of grey are used to avoid pseudo-contouring (Delp & Buda, 1985) and 25 levels each of red and purple. The scale is displayed beside Fig. 1C.

The grey-scale transformation is a point operation (Delp & Buda, 1985) described by the equation from Rosenfeld and Kak (1982a)

$$P_{new} = (P_{old} - a) \times (k - j)/(b - a) + j$$

where P_{new} is the new pixel value, P_{old} is the old pixel value, the old grey scale runs from pixel values a to b and the new scale from values j to k.

Once the decision has been made whether to use the pixel value from the anatomical or from the flow image, the point operation is carried out on the appropriate image. For the anatomical image, $a = 0$, $b = m$, $j = 0$ and $k = 63$; for the flow image $a = -n$, $b = +n$, $j = 64$ and $k = 113$. The result is to produce a composite image in which each pixel value corresponds exactly to one point on the colour scale.

RESULTS

Figure 1 shows the anatomical (Fig. 1A) and the flow (Fig. 1B) images and their combination to form the composite image (Fig 1C). The colour scale is displayed beside Fig. 1C.

Figure 2 shows the effect of the selection of the anatomical image threshold. Figures 2A, 2B, 2C and 2D show the effects of selecting levels of 20%, 25%, 30% and 35% of m, respectively. For all these images, the flow image noise threshold was 1% of n.

Figure 3 shows the effect of selection of the flow image noise threshold. Figures 3A, 3B, 3C and 3D show the effects of selecting values of 0%, 1%, 2% and 5% of n, respectively. For all these images the anatomical image threshold was 25% of m.

CLINICAL APPLICATION

To illustrate the scope of the information available from a cine display of composite images, Fig. 4 shows a series of eight coronal frames of a slice 1 cm thick, taken from a normal subject. They cover 350 ms at 50 ms intervals, Fig. 4A being 50 ms after the R-wave. Red signifies flow towards the head, purple towards the feet and the maximum velocity for the cycle is 1 m/s. The information will be discussed on a structure-by-structure basis.

Left ventricle and ascending aorta

During diastole, blood enters the left ventricle (Fig. 4E–H), flowing towards the feet. At the apex it turns round to flow towards the head. Following ejection into the aorta (Fig. 4B–D), the aortic valve closes and flow reverses in diastole (seen in purple in Fig. 4E). This flow reversal is due to blood moving back to dilate the sinuses of Valsalva and to enter the coronary ostia to supply the myocardium.

Left ventricular wall motion can be studied from the anatomical display of the left ventricular muscle shown in grey. The epicardial outline in this healthy volunteer moves relatively little, whereas the endocardial wall moves considerably. The reduction in cavity size with contraction is achieved through wall thickening in systole, corroborating angiocardiographic (Hughenholtz, 1969), echocardiographic (Gould et al, 1976; Henschke et al, 1983) and magnetic resonance evidence (Fisher et al, 1985; Rees et al, 1985; Underwood et al, 1986).

Figures 4D–G show the relationship of the rapid outward movement of the ventricular walls to the velocity of flow inside the ventricle.

Superior vena cava and right atrium

In Fig. 4 superior vena caval blood is seen returning to the heart; the slice is too far anterior for there to be any contribution from inferior vena caval blood. In this slice, the flow in the right atrium is always towards the feet, and is complex since chamber filling, emptying and change of size can be occurring simultaneously. The flow is less during systole (the dim purples of Figs 4A–D) and reaches its brightest when rapid ventricular filling is occurring (Fig. 4G). The significance of the brighter areas seen in the right atrium is unclear.

Pulmonary artery

The blood in the pulmonary artery is divided into a dim shade of red on the left and a dim shade of purple on the right (Figs 4B–D), consistent with streaming as it flows into the right and left pulmonary arteries. The dimness is due to the flow in this series of images being encoded in the head–foot axis, since the components of pulmonary artery flow in this axis are small.

DISCUSSION

Appropriate selection of the anatomical image and the flow image noise thresholds (Figs 2, 3) permits construction of readily interpretable images. For most pairs of anatomical and flow images of sufficient initial quality, we have found values of 25% of m as the anatomical image threshold and 1% of n as the flow noise threshold to be satisfactory.

Stationary blood at end-diastole gives a signal on anatomical images which may be above the anatomical image threshold, creating an artefact on the composite image. To avoid this, a method of differentiating stationary blood from solid anatomical structures is needed.

The flow image is originally constructed from a magnitude image which gives a very high signal for blood, thereby providing a criterion for the differentiation of blood from solid structures. The ideal method of producing composite images would, thus, be to produce them at the time of processing the flow data, so that anatomical, magnitude and thresholded flow images could be used.

The decision on whether to use a pixel from the anatomical or from the flow image would then depend on three thresholds. If a pixel were above the anatomical image threshold, the magnitude image would be examined. If the magnitude pixel were below a magnitude image threshold, the anatomical pixel would be used. If it were above this threshold the flow pixel would be used Were the flow pixel below the flow noise threshold, a value corresponding to zero flow would be inserted on the composite image

The image-processing program has been designed to allow the value of n to be supplied by the operator. This allows the maximum flow velocity for the entire cardiac cycle to be used rather than that for the current flow image, permitting a series of frames from different points in the cycle all to be scaled to the same maximum. By this means flow can meaningfully be followed on cine display

A common way in which computer cine displays work is by expanding to full screen frames each occupying a fraction of the screen (say one quarter) in rapid succession. This means that the screen must first be filled with quarter-sized images. Many programs average regions of images which they are contracting, in order to obtain the best estimate of the pixels in the smaller image. In the case of composite images this means that anatomical pixels (grey) would be averaged with flow pixels (coloured), yielding a value which may be in the grey or the coloured parts of the scale.

The effect of such averaging is to produce spurious white borders at the junction of grey and coloured parts of the image. This may be overcome by further processing of the composite image to produce a physically smaller image (128 x 128 pixels) in which the problem has been taken into account, reducing four pixels to one A choice of criteria is available, *e.g.* using the first of the four pixels, the maximum or the minimum of the pixels, a median filter (Rosenfeld & Kak, 1982b) or producing an average whose calculation excludes either flow or anatomical pixels.

Taking the first of the four pixels was tried as the simplest method, but this disposes of three-quarters of the information in the original image. The result is the production of ragged borders between flow and anatomy on the composite image and non-uniformity of velocity profiles, both of which reduce the ease of interpretation. A better approach is to take the maximum of the four pixels, as is done during signal acquisition in some echocardiographic systems (Garcia et al, 1981). This gives both smooth borders and smooth velocity profiles and it is the approach we have adopted for cine display.

The concept of colour display of flow information in the heart superimposed on a grey-scale image of anatomy has already proved its clinical usefulness (Miyatake et al, 1984, 1986a,b). The details of image processing with ultrasound and with magnetic resonance are, however, very different.

Magnetic resonance gives better spatial resolution, better soft-tissue discrimination and better portrayal of velocity data with 25 levels of velocity in each direction as opposed to eight for ultrasound (Miyatake et al, 1984). Aliasing problems do not exist with magnetic resonance provided that selection of the size and duration of the gradient pulse is appropriate (Bryant et al, 1984). The lower limit of sensitivity of the phase-mapping method is 1/25 of the maximum flow velocity selected, since this is the number of steps in the linear colour scale.

CONCLUSION

Cine display of composite images depicting both blood flow and anatomy aids interpretation of the wealth of clinical information available from magnetic resonance studies by portraying this information in a compact form. Its application to the anatomy and flow of the diseased heart will enhance our understanding of the physiology and the pathology of these disease processes. Application to the study of cardiac function following myocardial infarction, in cardiomyopathy, in valvular regurgitation, in septal defects, and in congenital heart disease will be instructive. The use of this composite display as a method of studying the improvement of function of the ischaemic heart following bypass grafting or percutaneous transluminal coronary angioplasty will be of use both as a research technique and in patient management.

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Book review

Cisternographic Anatomy of the Posterior Cranial Fossa. High resolution CT and MRI study. By R. G. M. de Slepte, J. Valk, A. H. M. Lohman and F. W. Zonneveld, pp. vii+172, 1986 (Van Gorcum, The Netherlands), Dfl 75.00.
ISBN 90-232-2224-5

Two Dutch radiologists, an anatomist and a physicist, have produced this work on the radiological anatomy of the subarachnoid cisterns of the posterior cranial fossa as demonstrated by computed tomography (CT) and magnetic resonance imaging. The introduction is followed by a concise chapter on the physical principles of the two imaging techniques. The next chapter is devoted to a well illustrated atlas of the normal anatomical appearances, with the CT and magnetic resonance images displayed below pictures of the corresponding cryosection of the skull and brain. Opposite each set of illustrations is a key to the anatomical features. The use of a black and white picture between the colour pictures and the radiological images is of great assistance in the interpretation of the radiological features.

Chapter 4 consists of a well illustrated description of the major cisterns and the smaller cisterns arising from these structures. The dimensions and frequency of their visualisation both in plain and intrathecally contrast-enhanced CT studies are given. Pathological enlargement and reduction in the size of the cisterns are discussed and considerable space is devoted to the appearances and mechanisms of the Dandy Walker malformation and its variants.

The normal and abnormal appearances of the intercisternal structures are discussed and illustrated. Line drawings of the anatomy are provided and many of the drawings show the plane of section necessary to demonstrate the vessels and cranial nerves crossing the cisterns. Also included in this chapter is a description of the use of enhanced CT scanning for the demonstration of cranial nerve compression by vascular structures in hemifacial spasm and trigeminal neuralgia, which is claimed to be the investigation of choice in these disorders.

The sixth chapter is devoted to the bony structures bounding the cisterns and deals with congenital and acquired anomalies of the skull base, fractures, tumours and the changes at the cranio-cervical junction in rheumatoid arthritis.

The final chapter deals with the brain-stem, cerebellum and upper cervical cord and includes various congenital abnormalities. Cerebellar hypoplasia of various types is described and illustrated and 12 pages are devoted to a very good account of the Chiari malformations. The final pages are devoted to syringomyelia and tumours of the brain-stem.

Throughout the book there are very comprehensive and up-to-date collections of references, but the illustrations are of mixed quality. This is probably a reflection of the practical difficulty in attempting to demonstrate fine structures, such as nerves, by these imaging techniques. Some of the magnetic resonance images are of poor quality and have probably been obtained using body coils. With the current use of surface coils, subsequent editions could well include better images.

The text is full of information which makes prolonged reading a little difficult, but repetition of information is at a minimum. I consider this book to be an essential reference and practical manual in all neuroradiological departments and it has earned its place in our department library on a single reading. The authors are to be congratulated for producing this work.

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Paget's disease of bone in Africans

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ABSTRACT

Fourteen cases of Paget's disease of bone seen in an African community over a 4-year period are reported. During a comparable 4-year period, no case of Paget's disease was seen in a busy radiology department of a teaching hospital in Nigeria. It is suggested that Paget's disease of bone may not be uncommon in some African communities and that the striking geographical variation in the incidence of this disease in Europe, America and elsewhere is applicable to Africa also.

All published reports on Paget's disease of bone emphasise its rarity in Africans. Because of the author's observation and the general clinical impression that this disease may not be uncommon in the Sierra Leonean, a prospective study was undertaken to assess the prevalence of the disease in a predominantly African community in Freetown, Sierra Leone.

MATERIALS, METHOD, RESULTS

During the period June 1978 to June 1982, all African patients attending the X-ray Department of the Connaught Hospital in Freetown with a radiological diagnosis of Paget's disease of bone were documented. These fourteen patients were interviewed as regards their symptoms and a detailed family history taken. Each patient had a full skeletal survey and serum alkaline phosphatase level estimation, and the results were recorded (Table I).

REPRESENTATIVE CASE REPORTS

Case 1

A 62-year-old man complaining of pain in the right knee for 2 years. A radiograph of the knee showed changes typical of Paget's disease involving the distal femur (Fig 1).

Case 7

A 74-year-old woman with long history of headaches as well as pain and stiffness, involving both hip joints, with limping Radiographs revealed advanced Paget's disease involving the pelvis and both femora with secondary osteoarthritic change in the hip joints (Fig. 2). The spine and skull were also involved.

Case 9

A 48-year-old woman who had been involved in a road traffic accident and had sustained a laceration of her scalp. Skull radiographs showed typical osteoporosis circumscripta, but no fracture (Fig. 3)

TABLE I

SUMMARY OF FINDINGS IN 14 CASES OF PAGET'S DISEASE

Case	Sex	Age (years)	Symptoms	Anatomical sites	Alkaline phosphatase level (normal 60–170) (IU/l)
1	M	62	Pain in right knee	Distal femur	120
2	M	54	None	Pelvis	75
3	F	72	Backache, pain in both hip joints	Lumbar spine and pelvis, left femur	245
4	M	63	None	Skull	80
5	M	49	Headaches	Skull	120
6	M	49	None	Pelvis	196
7	F	74	Pain in hip joints	Skull, lumbosacral spine and femora	140
8	M	56	Pain and deformity right femur	Pelvis, right femur with pathological fracture	440
9	F	48	None	Skull	190
10	M	59	Progressive enlargement of head	Skull, lumbar spine	485
11	M	70	None	Pelvis, right tibia	60
12	F	67	Backache	Dorsal and lumbar spine	75
13	F	52	Recurrent sinusitis	Skull, left clavicle, pelvis and femora	105
14	M	63	None	Right femur	105

Note: the skin colour of each patient was black

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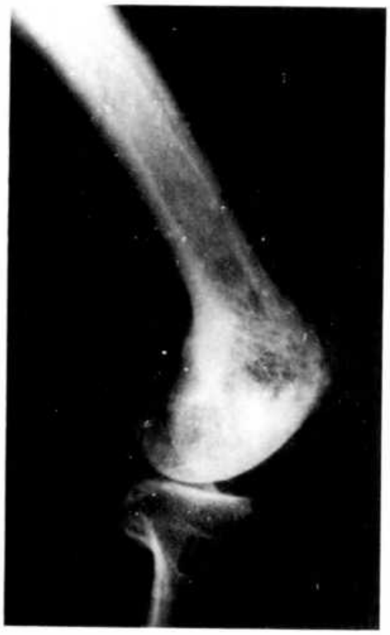

FIG. 1. *Case 1.*

Lateral radiograph of right knee showing Paget's disease of the lower femur. Note marked sclerosis, cortical thickening and accentuation of the trabecular pattern.

Case 11

A 70-year-old man was referred for a barium enema because of recurrent rectal bleeding. Marked bowing of the right tibia with increased temperature on palpation were observed. Radiographs confirmed clinical suspicion of Paget's disease (Fig. 4). The left side of the pelvis was also involved.

Case 13

A 52-year-old woman complaining of recurrent sinusitis. An occipito-mental view of the skull revealed advanced Paget's disease (Fig. 5). The pelvis and femora were also involved, as was the left clavicle.

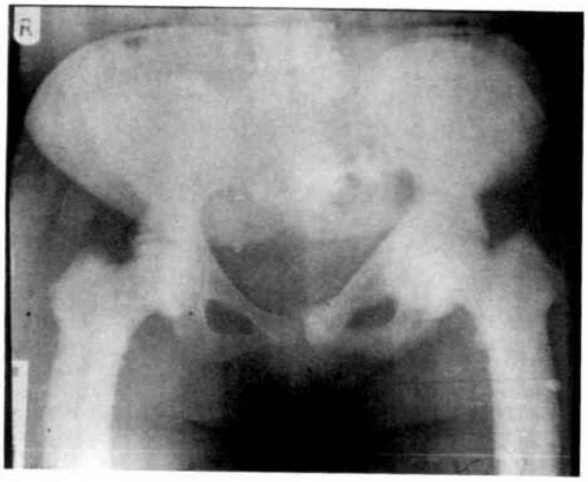

FIG. 2. *Case 7.*

Antero-posterior view of the pelvis. Changes of advanced Paget's disease involving the pelvis and upper femora. There is marked cortical thickening and coarse trabecular pattern. Osteoarthritic changes are shown in the hip joints.

DISCUSSION

Paget's disease of bone was first described in 1877 by Sir James Paget (Paget, 1877), who presented five cases of a bone disorder which he called "osteitis deformans". The disease is characterised by increased osteoclastic activity with resulting resorption of bone followed by subsequent osteoblastic activity with reactive bone formation (Merkow & Lane, 1984).

The aetiology of the disease remains unknown.

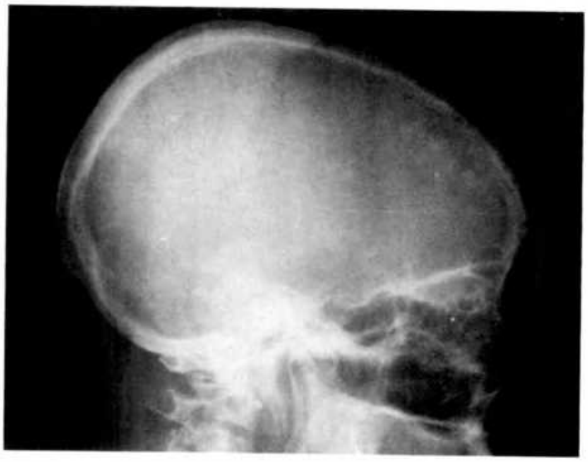

Fig. 3. *Case 9.*

Lateral view of skull. Note loss of bone density in the frontal and parietal regions (osteoporosis circumscripta).

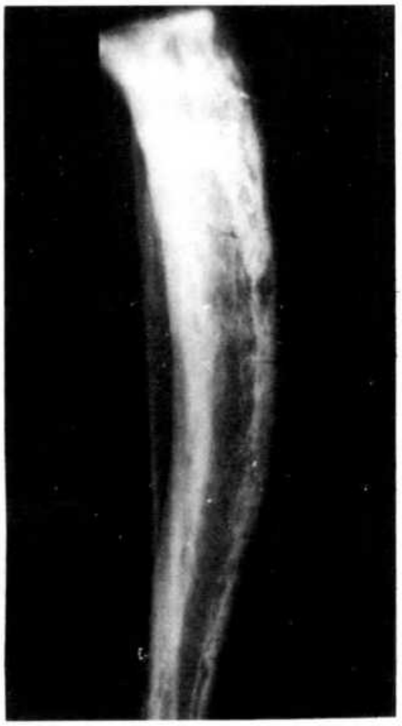

FIG. 4. *Case 11.*

Lateral view of right tibia. There is cortical thickening, trabecular accentuation and anterior bowing.

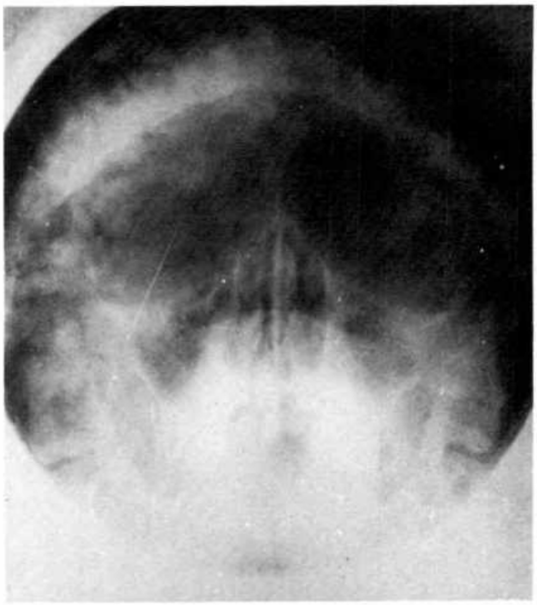

FIG. 5. *Case 13.*

Occipito-mental view of the skull showing advanced Paget's disease with "cotton wool" appearance.

Numerous hypotheses have been suggested, including inflammatory, neoplastic, vascular, genetic, and endocrine causes. Most authorities now agree that it is the result of a primary osteoclastic dysfunction, but the initiating factor is, as yet, undetermined. A viral aetiology has been proposed and evidence for this has been recently reviewed (Harvey, 1984).

There is a striking variation in the incidence of Paget's disease in different parts of the world. It is more common in Great Britain and Western Europe than in the United States and Scandinavia and has always been regarded as a very rare disease in Africa. Reeder and Palmer (1981) state that "it is such an uncommon bone disease in the tropics, that any suspected case should be carefully investigated to exclude all other possible causes of similar radiological changes, and perhaps the patient's ancestry should be checked as well".

Only five cases were seen in over 20 000 Nigerians who had been examined in the Radiology Department of the University College Hospital in Ibadan (Bohrer, 1970). Four cases have been reported from Senegal (Collomb et al, 1967). Pompe van Meedervoort and Richter (1976) reported nine cases in South African blacks, and three further cases in South African blacks were reported by Robertson and Thomas (1978). The disease is also rare in Asia, especially in India (Chakrabarty & Bhardwaj, 1963), Malaya and China. This paper documents the largest number of African cases so far reported.

In most reports men are more commonly involved than women, and in this series there were 10 men as against four women. Their ages ranged from 46 to 74 years, with a mean of 60 years. The diagnosis was an incidental finding in six patients with no symptoms referrable to the disease. The skull, pelvis, femur and lumbar spine were most frequently affected. Serum alkaline phosphatase level was elevated in six patients.

Although gene marker studies were not done because of lack of facilities, the physical appearances and family history of all 14 patients did not suggest any Caucasian admixture.

The striking geographical variation in the prevalence of Paget's disease of bone has been emphasised and its incidence may in fact vary in different parts of the same country (Rosenbaum & Hanson, 1969).

The 14 cases seen in Africans over a period of 4 years in 82 000 radiological examinations suggest that the disease may not be rare in some African communities. In a comparable 4-year period (1982–86) in a busy radiology department of a teaching hospital in northern Nigeria, the author did not see a single case of Paget's disease of bone in over 60 000 examinations. It therefore seems reasonable to conclude that the geographical variation in the incidence of the disease in other parts of the world is also applicable to the African continent.

It is also possible that the rarity of the disease in some African countries may be apparent rather than real. The population seen in most African hospitals is relatively young, whereas the disease is more commonly seen in the older age group. Also, most cases of Paget's disease of bone are first recognised radiologically, and neither radiologists nor radiological facilities are readily available in many African countries. If it is true that Paget's disease of bone is common in some African countries, further investigation would be valuable, as this may have relevance to the aetiology of the disease.

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Neurological morbidity of arch and carotid arteriography in cerebrovascular disease. The influence of contrast medium and radiologist

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ABSTRACT

A prospective study of 230 arch and carotid arteriograms in 229 patients with symptomatic cerebrovascular disease revealed that neurological morbidity was not significantly affected by patient age, nature of neurological symptoms, duration of procedure, volume of contrast medium or degree of arterial stenosis. The total neurological morbidity of 132 examinations carried out with non-ionic contrast medium (iohexol) was slightly lower than that of 98 examinations carried out with ionic contrast medium (meglumine and sodium iothalamate) but the difference was not statistically significant. However, the morbidity of 185 examinations performed by an experienced vascular radiologist was significantly lower ($p < 0.025$) than the morbidity of 45 examinations performed by a series of radiologists in training and the mean time required for the procedure was 18 min longer in the latter group ($p < 0.001$). These findings suggest that the neurological morbidity of arch and carotid arteriography in patients with cerebrovascular disease depends largely upon catheter technique and will not be significantly reduced by the use of non-ionic contrast medium.

The neurological morbidity of cerebral arteriography is significantly higher in patients with cerebrovascular disease than in patients with other neurological conditions (Mani & Eisenberg, 1978a; Faught et al, 1979, Earnest et al, 1984), but the reported rates vary. Faught et al (1979) found a range of cerebral complication rates between nil and 28% in 24 published surveys. In their own series of 147 patients with transient cerebral ischaemia or stroke, cerebral complications affected 12.2% of patients and were permanent in 5.2%. The same paper estimated an overall complication rate of 7% in 922 unselected patients having catheter studies and suggested that one third of these (2.3%) would be permanent. A review of 637 arteriograms in patients with symptomatic cerebrovascular disease by Earnest et al (1984) reported neurological complications in 4.2%, 0.63% being permanent. Most of these investigations were carried out with a single French gauge 5 catheter and few included an arch injection.

Mani et al (1978) reviewed the complications of 1702 cerebral arteriograms in patients with "suspected" cerebrovascular disease, but the criteria for this presumptive diagnosis were not stated. Neurological complications occurred in 1.6%, the incidence of permanent defects being only 0.07%. These comparatively low rates might be explained by the presence of patients without cerebrovascular disease in this study. In addition, since it was retrospective, some minor and temporary neurological defects could have been missed.

Some factors have been identified as increasing the neurological complications of arteriography in patients with cerebrovascular disease. Multiple ischaemic attacks (Faught et al, 1979; Earnest et al, 1984), recent stroke (Earnest et al, 1984), the age of the patient, the duration of the procedure and the volume of contrast medium (Mani & Eisenberg 1978b) have all been found to affect morbidity. Severe arterial stenosis was identified as a risk factor by Faught et al (1979), but not by Eisenberg et al (1980). Olivecrona (1977) found that the incidence of neurological complications was related to the difficulty of catheterising the carotid and vertebral arteries and Earnest et al (1984) reported a higher incidence of complications in examinations where more than one catheter had been used. Mani et al (1978) found that neurological morbidity depended upon the experience of the examining radiologist, being significantly higher in examinations performed by trainee radiologists. Raised serum creatinine levels were found by Earnest et al (1984) to increase the risk, and hypertension and diabetes mellitus were mentioned as risk factors by Faught et al (1979) and Earnest et al (1984).

The arteriograms in these reports were all carried out with ionic contrast media and, although most authors felt that the neurological complications resulted from catheter manipulation and were embolic in origin, the high osmolality of the contrast medium may have been a contributing factor. When non-ionic contrast media became generally available in 1982, animal experiments had already shown them to be less damaging to the normal blood–brain barrier when injected into the cerebral arteries and less toxic when introduced directly into the cerebrospinal fluid.

Clinical studies, however, had not shown these agents to have any beneficial effect on the neurological morbidity of cerebral arteriography. Skalpe et al (1980) found no difference between the neurological morbidities of cerebral arteriography with metrizamide and with meglumine metrizoate, and a review by Cronqvist (1983) of 13 trials involving 733 patients showed that, although non-ionic medium produced significantly less warmth and pain when injected into the carotid arteries, it had no effect on neurological morbidity. Kido et al (1985) have since reported a similar reduction in patient discomfort in a multicentre trial involving 277 patients, but found no significant effect on neurological morbidity.

Although digital subtraction angiography and ultrasound imaging have reduced the number of patients with suspected cerebrovascular disease submitted for carotid arteriography, it is likely that arteriography will have a continuing, if smaller, role in the future, as it demonstrates the extracranial and intracranial arteries more clearly than any other imaging technique. It is still important, therefore, to know whether the use of non-ionic contrast medium reduces the risk of neurological morbidity of carotid arteriography in this group of high-risk patients, or whether other factors are of greater importance.

METHODS AND MATERIALS

Between 1981 and 1984, 230 carotid arteriograms were carried out on 229 patients with symptomatic cerebrovascular disease: 112 patients had suffered one or more transient ischaemic attacks and 117 had developed strokes with more prolonged deficits but no serious residual disability. All were considered fit for reconstructive surgery if that proved appropriate.

The examinations were carried out under local anaesthesia and various forms of sedation administered by an anaesthetist monitoring the patient's blood pressure, electrocardiogram and level of consciousness during the procedure.

Catheterisation was carried out by the femoral route if possible, but the left axillary artery was used in 11 cases (two with ionic media, nine with non-ionic media) because of impalpable femoral pulses, previous arterial surgery, or failure to negotiate a severely diseased iliofemoral segment. Catheters were flushed with heparinised saline at 1-min intervals throughout the procedure. Care was taken to ensure that saline in the flushing syringe was not contaminated with aspirated blood and that small air bubbles were not trapped in the connectors and taps.

For the aortic arch, a French gauge 7 "pigtail" catheter was passed and radiographs were taken in the left anterior oblique projection after injection of 50 ml of contrast medium. Both right and left common carotid arteries were selectively catheterised in 223 examinations with a French gauge 7 femoro-cerebral catheter with a pre-formed loop. In two patients catheterisation of the right carotid was not attempted, as the arch radiographs showed severe stenosis ($> 75\%$) of the innominate artery In one patient the right common carotid was totally occluded and in another the carotid arteries were not catheterised as the purpose of the examination was to assess the patency of one carotid artery after surgery. Two examinations were abandoned (see below) and there was one technical failure where the right common carotid artery could not be catheterised owing to tortuosity of the innominate artery.

Carotid radiographs were taken in 30° antero-posterior half-axial "Townes" and lateral projections during the injection of 10 ml of contrast medium. Cut film, 36 cm × 36 cm, allowed the neck and intracranial vessels to be shown on one film with the same injection. Oblique radiographs were also taken if the carotid bifurcation had not been clearly visualised on the lateral radiographs, or if the middle cerebral artery was obscured by the skull base on the half-axial view.

During the procedure, patients were asked at frequent intervals to move fingers and toes, with a view to stopping the examination if a neurological defect developed, or if symptoms appeared. Two examinations were abandoned in these circumstances before completion: one patient became hemiplegic after the arch injection and another developed a right hemiplegia after the left carotid artery was injected with 10 ml of contrast medium.

The first 98 examinations (1981–82) were carried out with ionic contrast media: a mixture of meglumine iothalamate 52% w/v and sodium iothalamate 26% w/v (Cardio Conray 320, May & Baker) for the arch injection, and meglumine iothalamate 60% w/v (Conray 280, May & Baker) for the carotid injections. The following 132 examinations (1982–84) used non-ionic contrast medium: iohexol 300 mg I/ml (Omnipaque 300, Nycomed (UK) Ltd).

One hundred and eighty-five examinations were performed by a consultant radiologist (J.M.) with considerable experience of arteriography and the other 45 examinations were partly or completely performed by one of 10 registrars or senior registrars, all of whom had previous experience of selective abdominal arteriography. Patients in whom the examination posed a particular risk owing to recent stroke or frequent transient ischaemic attacks and those in whom the examination was likely to be technically difficult due to widespread arterial disease were allocated to the experienced radiologist.

After removal of the arterial catheter, patients were asked once again to move fingers and toes and the responses to simple questions were assessed. On return to the ward, usually 1 h after the procedure, a thorough neurological examination of every patient was carried out by the house officer responsible, and this was repeated 5 h and 24 h later. All patients for whom any neurological defect was reported within the first 24 h were assessed immediately, after 24 h and after 1 week and 1 month by a more experienced examiner (T.J.S. or G.D.P.).

TABLE I

NEUROLOGICAL MORBIDITY OF 230 ARTERIOGRAMS IN 229 PATIENTS' POSSIBLE RISK FACTORS

Possible risk factor	No neurological morbidity ($n = 204$)	Neurological morbidity ($n = 26$)	p
Patients			
Mean age (years)	61	67	NS (t)
Male	142	15	NS (χ^2)
Female	62	11	
Clinical presentation: TIA	99	13	NS (χ^2)
stroke	105	13	
Arteriographic technique			
Mean duration (min)	71	78	NS (t)
Mean volume of contrast medium (ml)	138	147	NS (t)
Contrast medium: ionic	85	13	NS (χ^2)
non-ionic	119	13	
Radiologist. experienced	169	16	< 0.025 (χ^2)
in training	35	10	
Arteriographic abnormalities*:			
None	51	3	NS } NS (χ^2)
Stenosis < 50% or irregular dilatation†	70	14	NS
Stenosis 50%–85%	39	3	NS } NS (χ^2)
Stenosis > 85% or occlusion	44	6	NS

NS = no statistical significance ($p > 0.05$).
Yates' correction applied to χ^2.
TIA = transient ischaemic attacks.
*The figure for arterial stenosis refers to the reduction in diameter of the most severely affected artery in the carotid tree between the aortic arch and proximal anterior and middle cerebral arteries. The narrowing was most severe in the carotid artery (common or internal) in 167 cases, the middle cerebral artery in five cases and the innominate artery in four cases.
†Irregular dilatation of the common or internal carotid artery probably due to an ulcerated atheromatous plaque.

RESULTS

Twenty-six examinations resulted in immediate neurological deficit, ranging from hemiplegia and blindness to minor alterations in muscle power or small visual-field defects, the latter sometimes unnoticed by the patient. Table I lists the possible risk factors present in these examinations. It shows a higher risk in females and a lower risk in patients without demonstrable carotid disease, but these differences are not statistically significant. The effect of the contrast medium, favouring the non-ionic, is small and not significant. On the other hand, the influence of the radiologist's experience is significant.

Table II and Fig. 1 record the persistence of neurological morbidity at intervals after arteriography for the whole group, and for four subgroups according to the type of contrast medium and the experience of the radiologist. Table III compares some technical

TABLE II

EARLY AND LATE NEUROLOGICAL MORBIDITY OF 230 CAROTID ARTERIOGRAMS: EFFECT OF CONTRAST MEDIUM AND EXAMINING RADIOLOGIST

Time after examination	No. of patients suffering neurological deficit	Contrast medium		p (χ^2)	Radiologist		p (χ^2)
		Ionic ($n = 98$)	Non-ionic ($n = 132$)		Experienced ($n = 185$)	In training ($n = 45$)	
Immediately	26 (11.3%)	13 (13.3%)	13 (9.8%)	NS	16 (8.6%)	10 (22.2%)	< 0.025
6 h	24 (10.4%)	12 (12.2%)	12 (9.1%)	NS	14 (7.6%)	10 (22.2%)	< 0.01
24 h	19 (8.3%)	10 (10.2%)	9 (6.8%)	NS	10 (5.4%)	9 (20.0%)	< 0.005
1 week	13 (5.7%)	7 (7.1%)	6 (4.5%)	NS	6 (3.2%)	7 (15.6%)	< 0.005
1 month	11 (4.8%)	5 (5.1%)	6 (4.5%)	NS	6 (3.2%)	5 (11.1%)	NS

NS = no statistical significance ($p > 0.05$).
Yates' correction applied to χ^2.

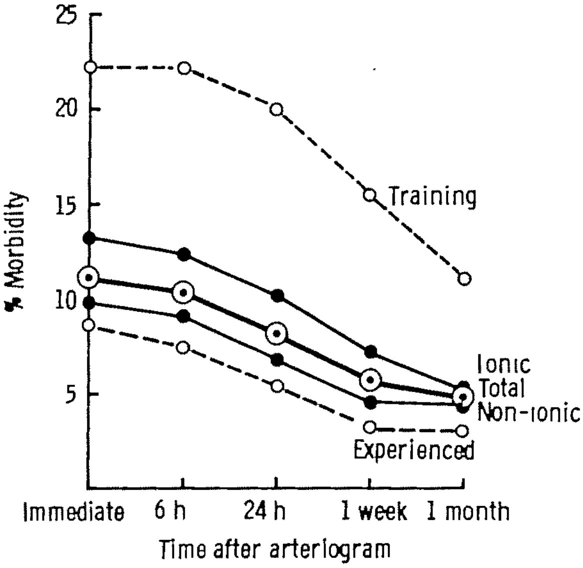

Fig. 1

Early and late neurological morbidity of 230 arch and carotid arteriograms: effect of contrast medium and radiologist's experience.

TABLE III

Technical aspects of 230 arteriograms performed by experienced and training radiologists

	Radiologist		p
	Experienced ($n = 185$)	In training ($n = 45$)	
Mean duration (min)	67.9	86.2	< 0.001 (t)
Mean volume of contrast medium (ml)	137	139	NS (t)
Ionic contrast medium	80	18	NS (χ^2)
Non-ionic contrast medium	105	27	

NS = no statistical significance ($p > 0.05$).

aspects of the arteriograms performed by the experienced and training radiologists and shows that examinations carried out by radiologists in training took, on average, 27% longer ($p < 0.001$).

Fifteen of the 26 initial defects had completely resolved within 4 weeks. Table IV lists those persisting beyond that time under the headings "major" (five patients) or "minor" (six patients), according to the degree of disability. The five patients with a major disability all had radiological evidence of carotid artery disease. In two cases the left internal carotid was occluded, in one case there was 70% stenosis of both internal carotid arteries and the other cases showed 40% and 20% stenoses of the right internal carotid artery.

Eight patients vomited during or immediately after the procedure; four had been examined with an ionic contrast medium and four with a non-ionic medium. There were no arterial complications at the puncture site requiring surgical treatment.

Discussion

Although there is an extensive literature on the neurological morbidity of cerebral arteriography in patients with cerebrovascular disease, accurate comparisons between this study and others are difficult owing to differences in patient selection, arteriographic technique and the procedure used to detect complications. The patients in this study all had symptoms indicating cerebrovascular disease, which is known to increase the morbidity of arteriography (Faught et al, 1979; Earnest et al, 1984), and it seems likely that the prospective nature of the study, with regular neurological assessments, detected temporary and minor defects that could have been missed in a retrospective review.

Our figure for major neurological morbidity at 1 month, 2.2%, is probably the most appropriate to compare with other studies, as patients with this degree of disability would have been detected retrospectively, but it is still likely to be higher than the figure for studies which included asymptomatic patients. It is close to the permanent morbidity of 2.3% estimated by Faught et al (1979) from a review of 24 published reports, but is much higher than the 0.63% recorded by Earnest et al (1984). This may be due to the fact that most of the examinations in the latter series were carried out with a single French gauge 5 catheter and few included an arch injection.

Although some of the neurological defects present at 1 month (Table IV) may eventually improve and some of the minor defects may resolve completely, the morbidity of our series is still high for a diagnostic procedure and emphasises the need for a safer technique which can be relied upon to produce good

TABLE IV

Neurological deficits present 1 month after arteriography: degree of disability

- Major (five patients)
  - Severe dysphasia, right homonymous hemianopia, mild right hemiparesis
  - Left central retinal artery occlusion with little residual vision
- Disabling diplopia, ataxia
  - Severe weakness of left hand, moderate left facial weakness
  - Severe weakness of right hand
- Minor (six patients)
  - Mild cerebellar ataxia of left limbs and gait
  - Mild left-sided weakness
  - Mild left arm weakness (three patients)
  - Unilateral extensor plantar response

diagnostic images of the extracranial and intracranial circulation.

The initial reason for monitoring these patients before and after arteriography was to balance the morbidity of the procedure at Charing Cross Hospital against the potential benefits of surgery. When non-ionic contrast media became generally available in 1982, their lower osmolality and neurotoxicity seemed to promise greater safety for otherwise high-risk patients, and the opportunity arose to compare the two types of media. With an adequately large series already completed for the ionic medium, further patient exposure to these was avoided by changing to non-ionic contrast medium for all examinations. This decision, made on ethical grounds, ruled out a randomised trial and the patients examined with ionic and non-ionic contrast medium formed consecutive groups. There was no change apparent to us in the criteria used to select patients for carotid arteriography in the course of the study

When other risk factors were investigated it became clear that neurological morbidity was largely determined by the experience of the radiologist ($p < 0.025$) and this was reflected in all categories of disability duration. The finding is in agreement with Mani and Eisenberg's (1978b) conclusion that the incidence of temporary neurological complications caused by cerebral arteriography in patients with vascular occlusive disease was significantly higher in training hospitals than in non-training hospitals and depended upon the experience of the examining radiologist. It was, nevertheless, an unexpected outcome of this study, as the examinations were supervised and as the radiologists in training had had previous experience of selective abdominal arteriography.

There was no difference between the two groups in the volume of contrast medium used (Table III), but the radiologists in training took, on average, 18 min longer to perform the examination ($p < 0.001$) and most of the extra time was spent manipulating the catheter around the origins of the carotid arteries while attempting selective catheterisation. This time was probably longer than the figures indicate, as the examinations expected to be technically difficult owing to severe disease of the iliac arteries or aorta, including those requiring an axillary approach, were all carried out by the experienced radiologist. Patients with identifiable risk factors, such as recent stroke or frequent transient ischaemic attacks, were also examined by the experienced radiologist and this may explain why there was no significant difference between the mean duration of arteriograms with neurological complications and the mean duration of those with no neurological complications (Table I).

The results of this study suggest that the neurological complications of cerebral arteriography are due to catheter manipulation and this is supported by the evidence of Earnest et al (1984), who found that the neurological morbidity of cerebral arteriography was significantly higher after examinations carried out with two or more catheters than after examinations carried out with a single French gauge 5 catheter.

The mechanism by which catheter manipulation produces neurological damage is uncertain. The most likely explanation is that the catheter dislodges fragments from atheromatous plaques situated in the aorta or innominate or common carotid arteries, and this would explain the higher neurological morbidity of cerebral arteriography in patients with symptomatic cerebrovascular disease compared with patients with other neurological conditions. Other sources of emboli include thrombus from the tip or side holes of the catheter, thrombus from the catheter lumen, or even small bubbles of air trapped within the tap or at the connections between the catheter, tap and syringe.

Although the aetiology remains uncertain, the results of this study suggest that the neurological morbidity of arch and carotid arteriography in patients with symptomatic cerebrovascular disease depends largely upon catheter technique and is not significantly affected by the type of contrast medium.

ACKNOWLEDGMENTS

We thank Dr John Salt, consultant anaesthetist, Charing Cross Hospital, for his help with the project We are grateful to Nycomed (UK) Ltd for supplies of iohexol (Omnipaque 300)

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Book reviews

Radiology of the Hand: a Diagnostic Synopsis of Many General Diseases By C J. P. Thijn, pp 302, 1986 (Springer-Verlag, Berlin), DM250
ISBN 3-540-15345-4 (Berlin)
0-387-15345-4 (New York)

The subtitle is *A diagnostic synopsis of many general diseases* and the author has, according to the foreword, used the hand as a window on skeletal radiology.

The text consists of sections devoted to one or more diseases, starting with a short general introduction, followed by a note on the radiographic features in the hand and those in other sites and concluding with a differential diagnosis. Each condition has a set of four to 10 references, normally including at least one to one of 20 standard monographs.

Each section is copiously illustrated with radiographs of the hand and other sites, and a notable feature is the inclusion of sets of radiographs of fingers illustrating five or more differential diagnoses Unfortunately, the text and sometimes the legends tend to be separated from the illustrations

The text is of rather uneven quantity and quality and there are several statements which are somewhat misleading, principally because of brevity. On the other hand, some of the lists of differential diagnoses include every possible condition, even if reported in very few patients, and it would have been helpful if the lists had been divided into common and uncommon differential diagnoses. I would also have welcomed a considerably more critical treatment in the text, even if this necessitated expansion.

The illustrations and the way they are arranged make the book well worth buying and the experienced radiologist will use the text to guide him to the other, more detailed descriptions in specialist monographs and journals The brevity of the text makes it an unsuitable book for trainees, but I would recommend it for every departmental library It is a useful complement to Poznanski's book, but is not capable of replacing it. I shall keep my copy and refer to it often

PETER DAVIES

Digital Subtraction Angiography in Clinical Practice. Philips Medical Systems, pp 196, 1986 (Philips Medical Systems, Best, The Netherlands), 100 Dutch Guilders (approx. £25).
ISBN 90-71546-01-2

This compact paperback book published by Philips Medical Systems has been written by one of the most experienced units in the field of clinical digital subtraction angiography (DSA) The authors represent a mixture of radiologists, clinicians and technical experts who clearly work very closely together to produce the best possible result in each individual patient. The book is written in a very conversational style, the authors describing their own experiences, problems and successes

Following a short introduction, the first major chapter is an excellent basic discussion on how to obtain good images from all areas of the body, and gives a large number of technical hints I feel the authors are uniquely unselfish in the amount of detail and advice given throughout this book and nobody using digital vascular imaging, or contemplating using it, should fail to read through this book and glean the technical hints that abound on just about every page. The following chapter is by an application specialist from Philips Medical Systems on the specific features of the equipment used in the department in Utrecht. There then follows a series of chapters, written by either radiologists or clinicians, discussing the role of DSA in carotid disease, aortic aneurysms, urological neurology, neuroradiology, bronchial and pulmonary disease, and peripheral vascular disease These chapters follow the same informal style, frequently describing specific cases that have been examined and the authors' personal experiences and feelings about the technique.

The final two chapters cover the economic aspects and the cost–benefit calculations for DSA, very important chapters for those readers wishing to convince their authorities that DSA represents a true investment

I have no hesitation in recommending this excellent, very readable and lavishly illustrated text on DSA; it is a must for every department using DSA and for all radiologists and radiographers involved in its use.

A P HEMINGWAY

1987, *The British Journal of Radiology*, 60, 123–125 FEBRUARY 1987

Limb muscle compression: an alternative technique for intravenous digital subtraction angiography

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ABSTRACT

A simple, muscle-compression technique to introduce a bolus of contrast medium from hand or foot injections for intravenous digital subtraction angiography (DSA) is described. Fifty millilitres of the non-ionic contrast medium iopamidol 300 was used for each projection. In 18 out of the 20 examinations an acceptably diagnostic arteriogram was obtained. It is suggested that the compression technique is a useful alternative for intravenous DSA when conventional venous access is impossible

Intravenous digital subtraction angiography (DSA), because of its virtually non-invasive nature, has become a routine first investigation in patients with suspected peripheral vascular disease; it is also useful in the assessment of surgical results as well as the investigation of post-operative vascular complications.

The usual method of introducing a bolus of contrast medium is either through a central line from the basilic or femoral vein into the right atrium; equally informative results may be obtained by introducing a short cannula into a peripheral vein in the region of the elbow (Lea Thomas & Treweeke, 1986). Some of these patients, particularly post-operatively or while undergoing a repeat examination, have thrombosed antecubital veins and recent incision in the region of the groin makes access to these sites impossible. Venous access is also often difficult in very obese patients.

Our standard method of demonstrating the iliac veins and inferior vena cava during ascending phlebography from a foot vein is by calf compression to produce a bolus (Lea Thomas & MacDonald, 1977); a similar technique shows the upper arm veins from hand injection when the upper limb is swollen (Lea Thomas, 1985). In this paper we describe the use of a limb muscle-compression bolus technique for intravenous DSA in patients with no readily accessible site for direct venous injections.

TABLE I

DETAILS OF PATIENTS

Case	Age (years)	Sex	Indication	Image quality
1	68	M	Calf claudication	Fully diagnostic
2	63	M	Patency of femoro-popliteal bypass graft and run-off	Fully diagnostic
3	61	M	Patency of femoro-popliteal bypass graft and run-off	Adequate
4	49	M	Calf claudication	Adequate
5	72	M	Demonstration of femoral false aneurysm, and	Inadequate (poor opacification)
6			Suspected stenosis at site of femoral aneurysectomy	Adequate
7	59	M	Patency of aorto bifemoral graft and right femoro-popliteal bypass	Adequate
8	58	F	Calf claudication	Fully diagnostic
9	42	F	Demonstration of popliteal aneurysm	Adequate
10	67	M	Patency of femoro-popliteal graft and calf run-off	Fully diagnostic
11	68	F	Exclusion of left subclavian artery stenosis or compression	Adequate
12	59	M	Suspected common iliac stenosis	Inadequate (bowel movement artefact)
13	40	M	Calf claudication	Adequate
14	48	M	Patency of aorto bifemoral graft and native femoral artery	Adequate
15	66	M	Suspected common iliac stenosis	Adequate
16	68	M	Patency of femoro-femoral crossover graft	Fully diagnostic
17	67	M	Patency of femoro-femoral graft and calf run-off	Fully diagnostic
18	61	M	Anatomy of abdominal aortic aneurysm	Adequate
19	60	M	Calf claudication	Adequate
20	55	M	Suspected brachial stenosis	Adequate

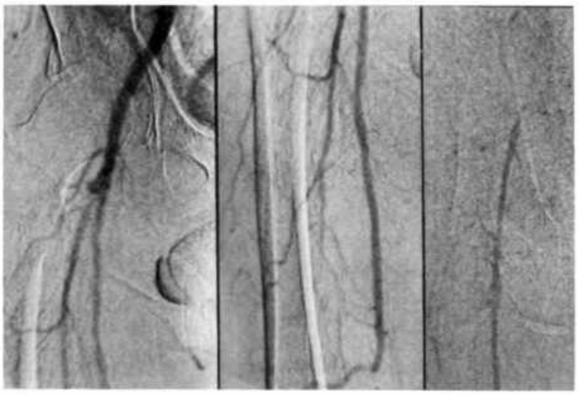

FIG. 1.

A fully diagnostic study in a 68-year-old man showing occlusion of the right superficial femoral artery with reconstitution in the adductor canal. Left pedal injection.

PATIENTS AND METHODS

Twenty examinations were performed in 19 patients with peripheral vascular disease. There were 16 men and three women, aged 40–72 years, mean age 60 years.

Technique

A self-fastening tourniquet is tightly applied above the knee or elbow; a 19 or 21 gauge butterfly needle is then introduced into a vein of the foot or hand; an additional tourniquet may be used temporarily to distend a vein. Fifty millilitres of iopamidol 300 (Niopam, E. Merck Ltd) is injected by hand as fast as possible. When the injection is complete the tourniquet is released and the calf or forearm squeezed to provide a venous bolus of contrast. Digital subtraction angiography imaging is then started at a frame rate of 1/s until the arterial tree has been optimally visualised, usually within 20 s from the start of limb compression. If the subtraction images are satisfactory the procedure is repeated, centring over another part of the arterial tree.

Minor complications occurred in two patients; in one there was extravasation at the venepuncture site and the other patient complained of slight pain around the ankle during the injection, although there was no evidence of extravasation. No serious complications, such as hypersensitivity, occurred.

RESULTS

Of the 20 examinations, six (30%) were fully diagnostic (Fig. 1) in that the arterial tree was diagnostically demonstrated in its entirety in the regions of interest. In 12 examinations (60%) the study was considered adequate, in that it answered the clinical query, but some of the arterial detail was obscured (Fig. 2). Two (10%) of the examinations were inadequate. The indications for the examinations and the results are shown in Table I.

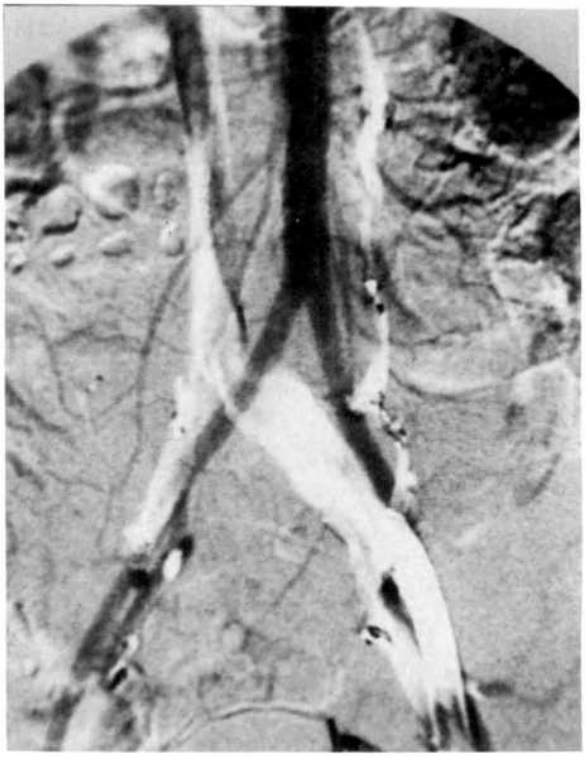

FIG. 2.

Investigation of a 40-year-old man with right-sided intermittent claudication. Left pedal injection. Residual contrast in the left iliac veins obscures the adjacent arteries but the iliac arteries on the right are adequately demonstrated. It is important to use the muscle-compression technique on the clinically normal limb if possible, to avoid venous overlap.

DISCUSSION

Low-osmolality contrast media are known to be painless on intravenous injection and have only minimal systemic side-effects, such as heat and nausea, which could give rise to movement artefact, important in intravenous DSA (Lea Thomas & Briggs, 1982, 1984). Furthermore, extravasation of these media due to vein rupture or needle displacement is not painful, although bruising, about which the patient should be warned, will occur. For these reasons low-osmolality contrast media should always be used for intravenous DSA. Iopamidol 300 was used in our series because of its low osmolality and relatively low viscosity (4.5 cP at 37° C), allowing easy injection by hand through small needles.

At least 50 ml of contrast medium is required for this bolus technique because, unlike direct injections into proximal veins, some of the contrast medium remains in the limbs and does not contribute to arterial opacification.

A specific source of image degradation related to this particular technique is the presence of residual contrast in the limb veins which may obscure some of the arterial detail. For this reason care must be taken not to use the muscle-squeeze technique in the limb of clinical interest if at all possible Venous contrast at the confluence of the iliac veins frequently obscures detail of the aortic bifurcation (see Fig. 2), but this problem may be overcome by remasking the DSA image sequence or taking an additional projection.

No attempt has been made to compare image quality with that obtained by more conventional intravenous DSA injection techniques because it would be impossible to obtain a matched group with the same pattern of arterial stenoses or vascular grafts. Nor would it have been ethically acceptable to use a compression technique in patients in whom conventional venous access is available.

We conclude, however, that the muscle-compression bolus technique is a useful alternative method for intravenous DSA when conventional venous access is impossible. In a few instances further investigation by arterial DSA or screen–film arteriography will be necessary.

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Book reviews

Diagnostic Radiology (An Anglo-American textbook of imaging). Ed by R. G. Grainger and D. J Allison, pp. 2234+index, 1986 (Churchill Livingstone, Edinburgh), £250
ISBN 0-443-02443-X

The Duke of Wellington is said to have written "Publish and be damned". The modern radiologist has altered this to "Publish or be damned" and with this third major textbook currently produced in the United Kingdom, salvation should be available for most of the current generation of radiologists who have turned their hand to writing.

This three-volume book has two principal editors, five section editors and 87 contributors (not counting Professor Steiner twice for the times that he appears in the list) Forty-one per cent are from the UK, 50% are working in the USA, and 9% are from mainland Europe, Canada or Brazil, so that the subtitle of the book *An Anglo-American textbook* is clearly justified

The three volumes are a pleasure to look at, with strongly bound royal-blue covers, an attractive type-face and profuse, good illustrations. Each section is completed with a list of references and suggestions for further reading so the reader can be assured that this book encompasses the radiological knowledge available up to the early years of the decade The number and reputation of the contributors has ensured that radiology is covered in all its aspects, and I have been unable to identify any glaring omissions. The index appears at the end of each volume, making cross-referencing reasonably easy.

The introductory section to each anatomical area and to the first volume will be necessary reading for radiologists early in their training, each section, that is, except the skeleton, where a decision has been made to assume that the normal is known. There is surprisingly little overlap from one section to another and it is good to see that in most cases ultrasound and computed tomography (CT) have been integrated into general radiology There are exceptions to this. There are separate sections on the use of radionuclides and CT in the skeleton and radionuclides in the head, and magnetic resonance imaging is, apart from the obligatory paragraph on its potential in the various sections, confined to the introductory section of the first volume

The editors and their contributors are to be congratulated on having produced a very good book that will immediately make its mark and should certainly be on the shelves of all teaching department libraries. I suspect that its sales to individuals will depend on the cost and content of the new edition of "Sutton", which comes from the same publisher and is said to be available soon

W. D JEANS

A Guide to the X-Ray Department, 2nd edit. By Myer Goldman, pp ix+94, 1986 (Wright Publishers, Bristol), £5 95
ISBN 0-7236-07651-6

This excellent little book was originally written to help nurses understand what various X-ray procedures involved, so that they could reassure anxious patients. In preparing the second edition the author has rightly recognised a much wider potential readership among professions supplementary to medicine, sixth-form science teachers and people in the equipment and medical-consumable industries.

An interesting and well illustrated historical introduction is followed by a brief explanation of X rays and the principles of the use of contrast media. There are eight chapters on the major anatomical subdivisions, each one describing the principal radiological examinations with clear examples of the results. The descriptions concentrate on aspects, such as fasting or the taste of a barium meal, which are probably the most common causes of anxiety to patients, and careful justification is given for each requirement.

There is a chapter on "Scanning" (actually incorrectly referenced on the contents page) which covers computed tomography, radionuclides, ultrasound and magnetic resonance imaging This is an area in which there is much confusion among lay people and putting all these techniques together is, paradoxically, a good way of distinguishing between them.

A chapter on other examinations gives short descriptions of various miscellaneous procedures Separate attention is given to the role of radiology in accidents and emergencies and, finally, a sensitively written chapter on protection places radiological hazards in the context of the assessment of risks generally.

The style throughout is clear and cheerful; the concise accounts of each procedure are easy to read. The book is liberally illustrated with diagrams and photographs of good quality In addition to its value for nurse education, the book is well worth recommending to friends, visitors or colleagues who would like to know a little more about the work of the X-ray department.

R. A. SHIELDS

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Evaluation of subjective assessment of liver function from radionuclide images

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ABSTRACT

The appearance of non-hepatic uptake in ^{99}Tc^{m}-colloid images is an important indicator of poor liver function. We undertook this study to evaluate the ability of experienced observers to assess liver function from radionuclide images. A simple model was used to simulate the changing distribution of ^{99}Tc^{m}-colloid in the liver, spleen and bone marrow as the liver function and mass were varied. Suitable images of these three organs were isolated from real studies and used as "templates" to create realistic simulated ^{99}Tc^{m}-colloid images, with the count densities of liver, spleen and bone marrow determined by the model. These images were presented in random order to several observers, who were asked to assess liver function. Comparison of the estimated with the true function shows that visual assessment is systematically inaccurate, with underestimation of poor function and overestimation of good function. It is also imprecise, especially for livers with only mildly impaired function. Observers were also affected by changing liver mass and were more likely to judge small livers to be abnormal. We suggest that objective assessment using a quantitative technique should be used as an adjunct to visual inspection for the evaluation of liver function.

In ^{99}Tc^{m}-colloid imaging of the liver, the three main sites of uptake are the liver, the spleen and the bone marrow. The distribution of injected activity between these organs is determined by their relative blood flows and extraction efficiencies. Any pathological reduction in blood flow to one of the three organs will result in decreased uptake of radiocolloid in that organ relative to the other two. For example, impairment of liver function due to diffuse liver disease (*e.g.* cirrhosis) can cause a reduction in effective liver blood flow (defined as the product of blood flow and extraction efficiency), with correspondingly increased uptake in the spleen and bone marrow.

Images showing such a distribution are considered to be useful indicators of diffuse liver disease (Baudouin et al, 1986) and the diagnostic criteria to be applied when evaluating liver function are well established (Simon et al, 1981). For subjective (visual) assessment of liver images, the main criteria are reduced liver uptake with no focal defects, increased splenic uptake with possible splenomegaly, and well defined bone-marrow uptake. This study was undertaken to evaluate the ability of observers to assess liver function from conventional radionuclide images.

We wished to investigate both the accuracy and the precision of subjective assessment, and to evaluate the effects of varying factors such as liver mass and effective blood flow. To provide control over these parameters, a simple compartmental model was devised to describe the distribution of radiocolloid between the liver, spleen and bone marrow. This model was used to create realistic computer simulations of typical ^{99}Tc^{m}-colloid images, with different values of the model parameters. These images were assessed visually by several experienced observers and the estimated liver function values compared with the known values of liver blood flow.

METHOD

Mathematical model

A compartmental model describing the clearance of injected colloidal activity from the blood pool to the liver, spleen and bone marrow is shown in Fig. 1. The model assumes that: (a) these organs are the only sites of uptake, and (b) the splenic extraction efficiency is sufficiently high for activity entering the liver via the splenic vein to be neglected.

Assumptions (a) and (b) are often made when measuring effective blood flow by determining the disappearance rate constant from surface counting results, and are justified elsewhere (Dobson et al, 1953; Vetter et al, 1954; Christie et al, 1967; Vetter, 1971). Liver dysfunction can be modelled by altering the effective blood flow, defined as the product of the liver blood flow and the extraction efficiency.

The differential equations generated by this model may be solved to give the activities at equilibrium in the liver, spleen and marrow, respectively:

$$A_L = A_0 \frac{l}{l+s+m} \qquad (1)$$

$$A_s = A_0 \frac{s}{l+s+m} \qquad (2)$$

$$A_M = A_0 \frac{m}{l+s+m} \qquad (3)$$

where A_0 is the injected activity (MBq) and l, s and m are the effective blood flows (ml/min) to the liver, spleen and bone marrow, respectively. Let the gamma-camera sensitivities for the liver, spleen and marrow be a, b and c (cps/MBq). These values take into account both geometric factors and attenuation, and hence depend on the imaging orientation. If a total of K counts are

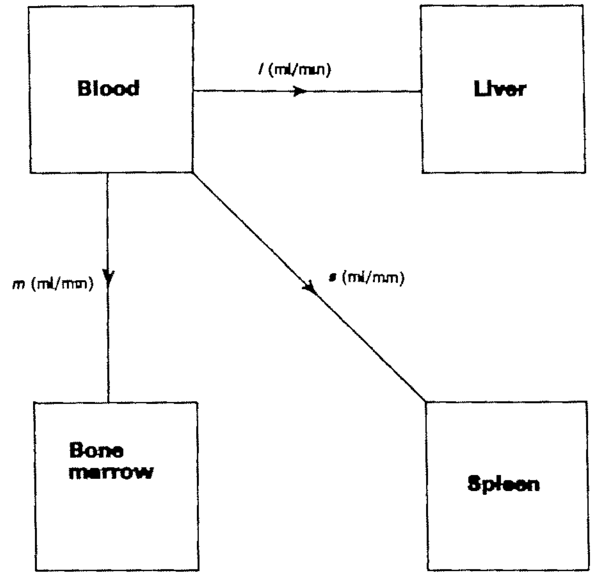

FIG. 1

The compartmental model describing the distribution of activity between the blood, liver, spleen and bone marrow

collected in an image, the number of counts contributed by each organ will be:

$$K_L = K\frac{al}{al+bs+cm} \tag{4}$$

$$K_S = K\frac{bs}{al+bs+cm} \tag{5}$$

$$K_M = K\frac{cm}{al+bs+cm} \tag{6}$$

The value of K was chosen to be 5×10^5, in accordance with our usual clinical practice. Values for the gamma-camera sensitivities in both anterior and posterior projections were obtained by estimating actual liver and spleen activities in a series of normal patients, using the geometric mean of opposed views (Fleming, 1979) and comparing these with the observed count rates from the three organs. The remaining parameters are the effective blood flows to the organs, l, s and m (ml/min). Values for effective hepatic blood flow have been estimated by several authors (Bradley, 1949; Christie et al, 1967; Pirttiaho & Pitkanen, 1977) for both normal patients and patients with cirrhosis. The total effective blood flow to the liver may be expressed as:

$$l = l_0 M \tag{7}$$

where l_0 is the specific effective blood flow (ml/min/g) and M is the liver mass (g). This allows us to vary independently both liver function and size

Values for effective splenic blood flow and splenic size have also been estimated by several authors (Henderson et al, 1981; Peters et al, 1984). Results obtained from patients with cirrhosis (Williams et al, 1968; Blendis et al, 1970) suggest that splenic blood flow and mass can increase by up to three times the values found in normal subjects. To take account of this effect, the splenic mass and blood flow were allowed to increase linearly with decreasing specific effective liver blood flow, up to a maximum at the most severe liver dysfunction of approximately three times the normal value.

No data have been obtained on effective blood flow to the bone marrow, so this was assumed to be constant and equal to the normal splenic blood flow. This assumption was justified by calculating the predicted disappearance rate of ^{99}Tc^m-colloid from the blood, and comparing this with observed values (Miller et al, 1979). Good agreement was obtained for the chosen values of liver, spleen and bone-marrow blood flow.

Values for all parameters used are shown in Table I. Although care was taken to choose realistic values, the absolute values of the parameter estimates are not crucial. The ultimate justification is that images produced by the model should be good representations of the range observed in clinical practice.

TABLE I

VALUES FOR THE MODEL PARAMETERS

Parameter	Symbol	Units	Values used
Liver specific effective blood flow	l_0	ml/min/g	0.16–1.04
Liver mass	M	g	900–1900
Splenic effective blood flow	s	ml/min	160–400
Marrow effective blood flow	m	ml/min	160
Gamma-camera sensitivities			
Liver	a	cps/MBq	70/44 (ant./post.)
Spleen	b	cps/MBq	35/88 (ant./post.)
Bone marrow	c	cps/MBq	47/60 (ant./post.)
Total counts in image	K	—	5×10^5

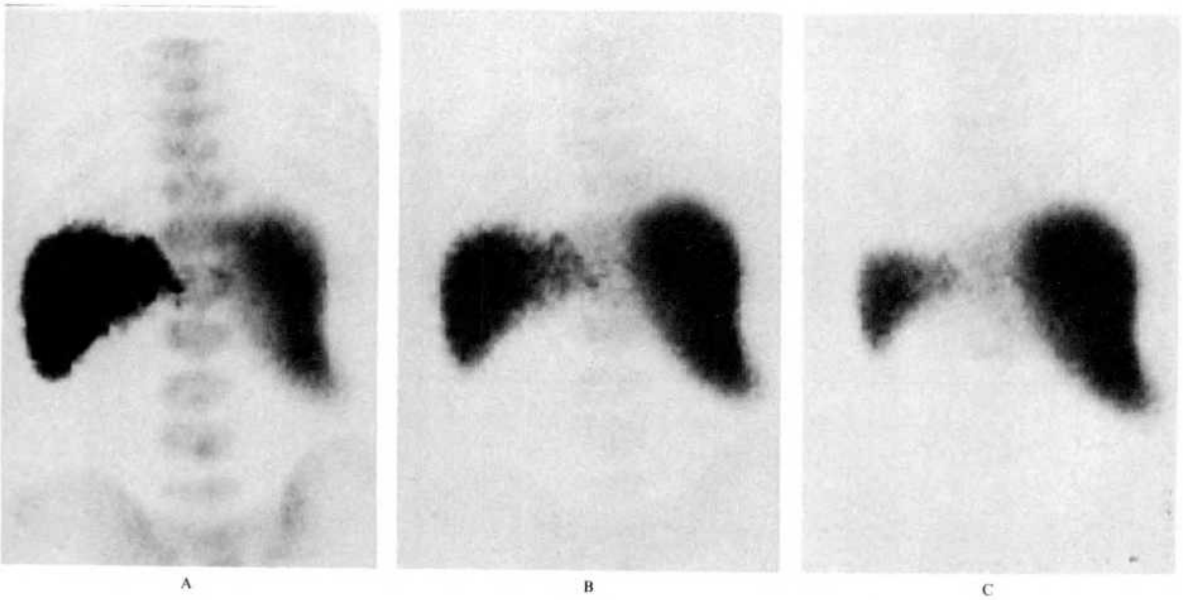

FIG. 2.

Simulated posterior images showing (A) severe dysfunction, (B) intermediate function and (C) unequivocally normal function.

Simulated images

The mathematical model described above was used to generate a series of simulated images in both anterior and posterior projections, with varying values of l_0 and M. Three isolated images showing only liver, spleen and bone marrow were obtained from real images and were used as organ "templates". These were chosen from normal studies and the relevant organ isolated using a simple region-of-interest masking technique. Digital images obtained at 128 × 128 resolution were used. Separation of a bone-marrow template from liver and spleen activity proved difficult, especially in the anterior projection. Bone-marrow templates were therefore obtained from a normal bone scan performed using ^{99}Tc^{m}-MDP.

Once values for l_0 and M were chosen, the total number of counts in the simulated image to be contributed by each of the three organs was calculated using Equations 4, 5 and 6. Each template was individually scaled to contain that number of counts. The liver and spleen templates were also spatially stretched using a linear factor proportional to the cube root of the liver and spleen mass, respectively. The three template images were then summed to give a realistic simulation of a ^{99}Tc^{m}-colloid image, with known values of liver mass and specific effective blood flow.

Twelve values of specific effective blood flow were considered, covering a range representative of severe liver dysfunction (0.16 ml/min/g) to unequivocally normal function (1.04 ml/min/g). For each value of specific effective blood flow we considered six masses, ranging from 900 g to 1900 g, consistent with reported values for the normal range of liver mass (Pirttiaho & Pitkanen, 1977; Henderson et al, 1981). Both anterior and posterior images were generated for each of the 72 combinations of liver mass and function.

Splenic blood flow and mass for livers with normal function were taken to be 160 ml/min and 200 g, respectively (Williams et al, 1968; Blendis et al, 1970). As discussed in the previous section, these values were increased linearly with decreasing liver function, up to maximum values of approximately 400 ml/min and 500 g. However, it was felt that a perfect correlation between liver function and splenic size was unrealistic, and so a random variation in splenic mass (Henderson et al, 1981; Peters et al, 1984) was superimposed on this linear trend.

Subjective assessment

Each of the 72 pairs of simulated images was displayed on photographic film with anterior and posterior images side by side, as consistent with normal practice. The images were presented in random order to seven observers (five physicists working in nuclear medicine and two radiologists), who were provided with visual analogue scales to mark their assessment of liver function. A training set was provided, representing severe liver dysfunction, unequivocally normal function, and intermediate function (Fig. 2). The corresponding points on the analogue scale were also shown, thus calibrating the scale. Each observer response indicating a point on the analogue scale could, therefore, be converted to a numerical assessment of liver function. Specific effective blood flow is a continuous variable,

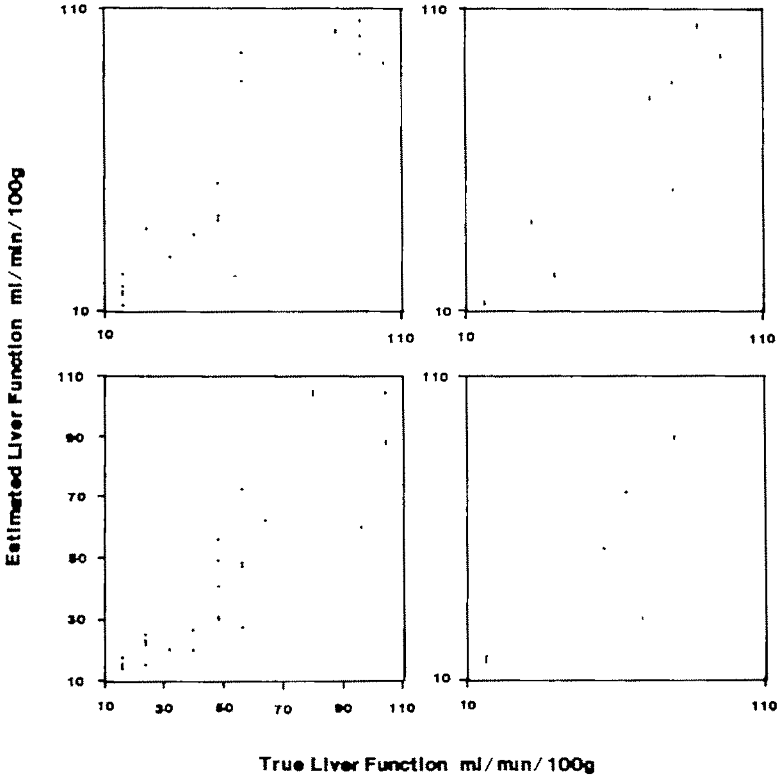

FIG 3.

Comparison between the visual assessment of liver function and true liver function for four observers.

and this method of assessment gave observers the freedom necessary to indicate any point from a range of function values.

RESULTS

Individual observers

Each observer generated 72 estimates of liver function, which were converted to numerical values (ml/min/g) using the calibrated scale. Assessments from four of the observers are compared with the true liver function values in Fig. 3. A perfect correlation between estimated and true function is hardly to be expected In fact, all observers showed evidence of a sigmoidal distribution about a linear trend, suggesting that observers tend to categorise their visual assessments of liver function into "normal" or "abnormal" and have difficulty in adapting to a continuous distribution of function values. Accuracy of visual assessment is therefore a non-linear function of liver blood flow, with underestimation of relatively poor function and overestimation of relatively good function.

Pooled data

The significant spread of liver function estimates at each value of true liver function was shown by all seven

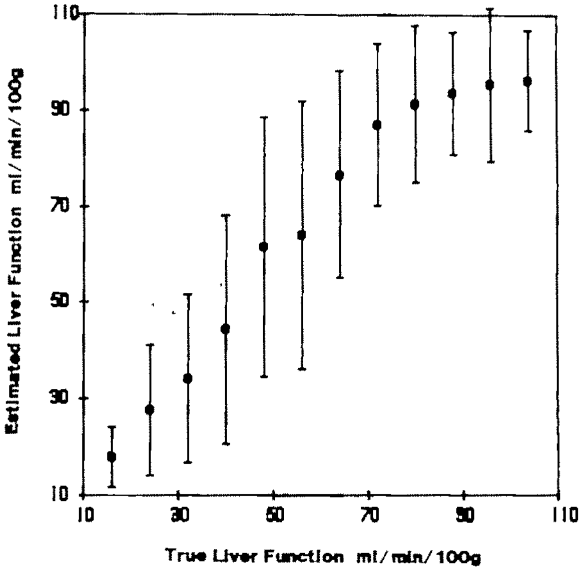

FIG 4.

Mean estimated function for all seven observers compared with the true liver function. Error bars show one standard deviation Note the sigmoidal trend and the lack of precision for intermediate true function values

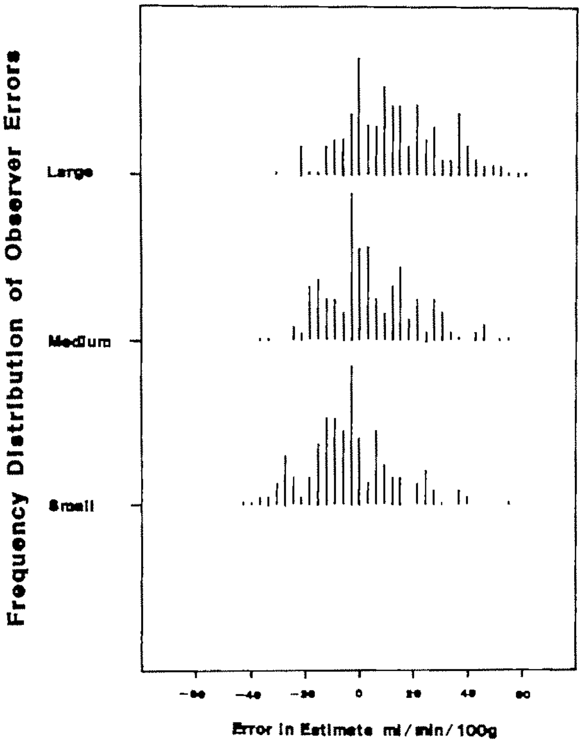

FIG. 5

Histograms showing the frequency distribution of differences between visually estimated and true function for small, medium and large livers.

observers, indicating that reproducibility (or precision) in the visual assessment of liver function is poor, especially for livers with intermediate function. Figure 4 shows the pooled mean and standard deviation of estimated function for all observers. The sigmoidal trend is clearly apparent, as is the poor precision for true liver blood flow in the range 0.4–0.8 ml/min/g.

Effect of liver mass

The effect of liver mass on the visual assessment of liver function can be seen by examination of the differences between estimated and true liver function values. Each of the seven observers made 72 estimates and so 504 differences (or "errors" in the estimate of function) are available. These data are plotted in Fig. 5 as histograms showing the frequency distribution of the errors, separated into three groups according to liver mass. A clear trend towards positive differences (*i.e.* increasing estimated function) occurs with increasing liver mass. The distribution of differences is approximately normal within each group and hence the variance ratio test may be applied. Differences between the three groups were highly significant ($p<0.01$) for data pooled into either three groups or six groups by liver mass.

DISCUSSION

The ability of observers to detect focal lesions in radionuclide images has been assessed using actual images from normal subjects with superimposed simulated abnormalities (Houston, 1980; Pitt & Sharp, 1985). We have used a similar approach to study the performance of observers when assessing liver function. A simple model was combined with normal liver, spleen and marrow templates to generate realistic simulations of radionuclide liver images with varying degrees of liver dysfunction.

The results obtained when observers relied on visual assessment alone suggest that precision (and hence reproducibility) of assessment is poor, unless the function is either entirely normal or grossly abnormal This observation is consistent with the evidence presented by Wasnich et al (1979), who showed that images with intermediate values of liver/spleen ratio were often classified incorrectly by visual inspection. Observers in our study were also confused by variation of liver mass without alteration in specific effective blood flow and were significantly more likely to judge small livers to be abnormal.

Quantitative techniques have been shown to improve greatly the detection of new bone lesions when compared with visual assessment alone (Pitt & Sharp, 1985), with the obvious problem that a region must first be identified as suspicious before it can be analysed by a manual region-of-interest technique Quantitative techniques for the assessment of liver function do not require defects to be localised in this way and a variety of methods have been proposed for objective analysis using liver/spleen ratios (Eddleston et al, 1969; Wasnich et al, 1979). Most of these use the ratio of count densities in simple regions which can be defined reliably and even automatically (*e g.* a square array of 10 × 10 pixels centred over the maximum count density in each organ in the posterior view). We have shown that experienced observers estimating liver function using visual assessment alone are prone to both systematic and random error. Our results suggest that some form of objective measurement should be used as an adjunct to visual inspection, especially when liver function appears to be only mildly impaired.

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Comparison of low-osmolar contrast media in paediatric cardiac angiography

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ABSTRACT

Sixty-two children investigated by cardiac angiography for a wide spectrum of congenital heart disease were randomly assigned to one of two groups, one for iohexol, 350 mg I/ml (Omnipaque, Nycomed UK Ltd) and one for iopamidol, 370 mg I/ml (Niopam, E. Merck Ltd) Changes in systolic pressure, end-diastolic pressure when the injection was made into a ventricle, heart rate and rhythm and plasma osmolality were assessed at 1 min and 3 min after the injection of contrast medium The angiograms were subjectively assessed for angiographic quality. No significant differences were detected between the two groups

Many studies have been undertaken comparing the non-ionic low-osmolar contrast media with ionic contrast media in both peripheral (Fletcher, 1982) and cardiac (Cumberland, 1981) angiography. These comparisons have also been performed in paediatric angiocardiography (Partridge et al, 1980; Baltaxe et al, 1983; Hellström et al, 1983) These studies concluded that there is less alteration in parameters such as heart rate, blood pressure and myocardial contractility with the low-osmolar non-ionic contrast media. Plasma osmolality and plasma volume changes have been shown following hyperosmolar contrast-medium injections (Iseri et al, 1965) and the high-osmolality of conventional contrast media is responsible for a number of major adverse reactions (Grainger, 1980). These changes are less marked with the low-osmolar contrast media (Hine et al, 1985), which have an osmolality about one-third that of the conventional contrast media and the new contrast media produce markedly less adverse effects (Grainger, 1980). A recent study has compared three low-osmolar contrast media in adult cardiac angiography and showed no difference in subjective side-effects (Peck et al, 1985). This study was undertaken to compare the use of the contrast media iohexol, 350 mg I/ml (Omnipaque, Nycomed UK Ltd), and iopamidol, 370 mg I/ml (Niopam, E. Merck Ltd), for paediatric angiography using a random selection of patients and blind assessment of results.

METHOD

Sixty-two children, aged 6 weeks to 10 years, undergoing cardiac catheterisation and angiography for a wide spectrum of congenital heart disease, including sick infants and those with cyanotic heart disease, were randomly allocated into two groups, one for iohexol 350 and one for iopamidol 370. The choice of contrast medium was made by the nurse in charge of the case drawing a card and selecting the contrast medium for the pump and hand injections without the knowledge of the operator. All examinations were undertaken under general anaesthesia. Each group contained 31 children. For the purpose of the study, data relating to the first angiographic injection, either into a ventricle or great artery, were recorded. In many cases subsequent injections of contrast medium were made, but these are not included in the study. The age and weight of each child and volume of the first injection were recorded. A 10 s electrocardiogram (ECG) tracing and pressure recording at the injection site were obtained before the angiogram, during the injection, and at 1 min and 3 min after injection. Blood samples for plasma osmolality were also obtained before and at 1 min and 3 min after the injection of contrast medium. Subjective assessment of angiographic quality was made for each angiogram.

RESULTS

The mean age (iohexol group, 42.3 months; iopamidol group, 48.6 months) and weight (iohexol group, 14.0 kg; iopamidol group, 14.2 kg) were similar and there was no statistical difference between the groups. There was also no significant difference in the volume of contrast medium injected (20.8 ml, 1.59 ml/kg iohexol; 19 6 ml, 1 58 ml/kg iopamidol). The left ventricle was the most common site of injection in both groups (17 cases in the iohexol group; 16 cases in the iopamidol group), other sites being the right ventricle, aorta and pulmonary artery.

Heart rate

Before injection of contrast medium there was no significant difference in heart rate between the two groups (113.9 beats/min, iohexol group; 107.3 beats/min, iopamidol group, $r = 0.85$). No significant change in heart rate occurred in the iopamidol group at either 1 min or 3 min after injection. In the iohexol group there was a statistically significant, but clinically unimportant, decrease in heart rate at both 1 min and 3 min.

Seven children in the iohexol group had ventricular ectopic beats (median frequency 2 beats) (10 s recording). One child in the iopamidol group had an episode of ventricular tachycardia after the injection and eight other children in this group had ventricular ectopic beats (median frequency 3.5 beats). These differences do not reach statistical significance.

Systolic blood pressure

Baseline systolic blood pressure was similar in both groups (92.6 mm Hg, iohexol group; 99.2 mm Hg, iopamidol group; $t' = 0.91$). Significant, but clinically unimportant, rises in blood pressure were recorded at 1 min (3.3%, iohexol group; 3.6%, iopamidol group; $p < 0.01$) and at 3 min (5.4%, iohexol group; 4.7%, iopamidol group; $p < 0.001$). There was no statistically significant difference between the groups at either time.

End-diastolic blood pressure

End-diastolic blood pressure was analysed in absolute rather than percentage terms where the injection was made into a ventricle. The mean baseline pressures were 4.0 mm Hg (iohexol group) and 5.4 mm Hg (iopamidol group) and large proportional increases were registered for both media at 1 min and 3 min, but there was no significant difference between the groups at either time.

Plasma osmolality

For both groups there was a highly significant increase in plasma osmolality of about 3% of baseline at 1 min after the injection. The mean values for both groups at 1 min rose above the upper limit of normal plasma osmolality (295 mosmol/kg H_2O). There was a reduction towards normal by 3 min but this still represents a significant increase above baseline (1.1%, iohexol group; 1.7%, iopamidol group; $p < 0.001$). At neither time was there any significant difference in response to the media.

Angiographic quality

The angiograms were subjectively assessed by one author (B.C.O.) without prior knowledge of the contrast medium used. There was no appreciable difference in angiographic quality between the two groups.

DISCUSSION

The results of this study are consistent with other investigations and show only small and statistically insignificant changes in heart rate, systolic and end-diastolic pressure. Although there was no significant difference between the groups, in the iohexol group there was a statistically significant, but clinically unimportant, decrease in heart rate at both 1 min and 3 min. Bradycardia has been a major problem with ionic contrast media but has been observed to occur to a lesser degree with low-osmolar contrast media. In both groups ectopic beats occurred on injection. One child in the iopamidol group had an episode of ventricular tachycardia but converted spontaneously to sinus rhythm. Arrhythmias may occur when a cardiac chamber is catheterised or when an injection is made. The occurrence of an episode of ventricular tachycardia in one child is unlikely to be related to the nature of the contrast medium injected. There was no significant difference in the number of ventricular ectopics experienced in the two groups. Both the systolic and end-diastolic pressures showed a rise at 1 min and at 3 min, but again there was no statistical difference between the two groups and these findings accord with Folke et al (1985) who showed a significant rise in left ventricular end-diastolic pressure, but a slight fall in systolic blood pressure at 1 min.

Plasma osmolality showed a significant rise of 3% over baseline at 1 min and a partial return to normal by 3 min. The osmolality of these contrast media, although much lower than their non-ionic counterparts, is still significantly greater than that of normal plasma (iohexol 350, 780 mosmol/kg; iopamidol 370, 790 mosmol/kg; plasma, 285–295 mosmol/kg H_2O). This accounts for the immediate rise in plasma osmolality at 1 min with redistribution of extracellular fluid resulting in a return towards normal by 3 min.

CONCLUSION

The non-ionic low-osmolar contrast media iohexol and iopamidol have been compared in paediatric angiocardiography. No difference was shown in the physiological parameters measured in this study or in angiographic quality. Because of the often precarious cardiovascular state of children undergoing cardiac angiography for congenital heart disease the non-ionic contrast media are preferable to ionic contrast media, but there is no reason to choose either of these media preferentially.

ACKNOWLEDGMENTS

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Book reviews

Ultrasound Annual 1985. Ed. by Roger C Sanders and Michael C Hill, pp. 382, 1985 (Raven Press, New York), $76.50.
ISBN 0–88167–143–6

Roger Sanders and Michael Hill have again produced an ultrasound annual which contains contributions exploring the outer limits of current ultrasound experience. They have recruited authors with experience in many different but topical areas and the range of subjects covered in the 11 chapters is particularly wide Everyone, from ultrasound physicists to radiographers in training, would find something of interest in this volume.

The book starts with a short chapter describing the principles of "computed sonography" as used by Acuson. This is certainly a chapter of interest for those involved in the physics of ultrasound, as is a slightly longer contribution from Shawker and his colleagues at The National Institute of Health, who present a review of progress in the area of ultrasonic tissue characterisation. The final chapter is also concerned with ultrasound physics as it affects human biology and reproduction This contribution is particularly relevant as the effects of the use of ultrasound have promoted recent discussion and it is reassuring, therefore, to find in a 20-page chapter a balanced assessment of the available data which concludes that "there is no validated experimental evidence on which the safety of current usage of diagnostic ultrasound can be reasonably questioned "

The clinical ultrasonographer will find all he needs to know about examination of the urinary tract and adrenal glands in infants in an excellent chapter written by Anna Nussbaum and Roger Sanders. The editors have collaborated on the production of an excellent, clinically orientated chapter on sonography of the solitary liver mass These are the only mainstream clinical presentations, but there are interesting and relevant contributions on the examination of the infantile hip and the use of ultrasound in orthopaedics and soft-tissue extremities. The musculo-skeletal theme is continued in a chapter devoted to the examination of the spine which includes some truly excellent images of the fetal and neonatal spine. There are also chapters describing the fetal biophysical profile and the contribution of ultrasound to invasive fetal therapy

The subjects covered in this volume are many and varied and those with a practice which includes ultrasonography of swine, horses and "small companion animals" will find something of interest in a fascinating chapter from the College of Veterinary Medicine in Minnesota!

The *Ultrasound Annual 1985* is well illustrated and an invaluable purchase for any departmental library. If the average ultrasonographer were to read nothing beyond this volume then he would still be able to offer a useful opinion on the current developments in ultrasound

D. M. KING

Genito-Urinary Ultrasound. Clinics in Diagnostic Ultrasound 18
Ed by Hedvig Hricak, pp. 295, 1986 (Churchill Livingstone, New York), £29 90.
ISBN 0–443–08409–2

This is a welcome addition to the popular series of clinics, covering ultrasound of the genito-urinary tract *in utero* and throughout life There are five chapters on renal imaging; the remaining six discuss its role *in utero*, in paediatrics, transrectal sonographic urodynamics, prostatic and scrotal ultrasound and also Doppler ultrasound in urology

The book is easy to read, well indexed and nicely illustrated. The applications of ultrasound are discussed in relation to specific clinical problems and there is a good balance between the clinical and sonographic features. Despite stressing the importance of ultrasound, there is a reasonably good discussion of the role of ultrasound in relation to other imaging modalities such as computed tomography and magnetic resonance imaging.

There are a few printing errors but none that detract from the value of the book, which I can recommend not only to those who perform ultrasound but also to their clinical colleagues and radiologists with an interest in genito-urinary medicine.

M PHELAN

1987, *The British Journal of Radiology*, 60, 137–141 FEBRUARY 1987

Ultrasound findings in children with cystic fibrosis

By J. M. McHugo, F.R.C.R., C. McKeown, M.R.C.P., M. T. Brown, F.R.C.R., P. Weller, F.R.C.P. and K. J. Shah, F.R.C.R.

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ABSTRACT

The results of a prospective study using ultrasound to assess abdominal complications in 76 children with proven cystic fibrosis are reported. Fifty-six patients (74%) had normal liver ultrasound scans. The most striking abnormality was an irregular, inferior edge to the liver occurring in 85% of abnormal liver scans and in 70% there was corresponding clinical and biochemical evidence of abnormal liver function. This finding has been only briefly mentioned before. Increased reflectivity in abnormalities of the pancreas and gallbladder is also described.

Cystic fibrosis (CF) is a common, genetically determined disease seen in caucasian children with an estimated birth prevalence of approximately 1 : 2000 (Andersen, 1958). Patients are now living longer (Park & Grand, 1981) because of better management of their respiratory and pancreatic disease, and with this increased life span there has been an increase in the incidence of hepatobiliary complications. These have important implications for the management and prognosis of such patients. The frequency of liver disease in CF is difficult to assess as most studies have employed different investigations to detect hepatic involvement in varying age groups. Thus 47% showed hepatic involvement post-mortem (Oppenheimer & Esterly, 1975a) whereas only 17.8% had abnormalities on liver biopsy (Dietzsch et al, 1980). More recently, ultrasound has been used to assess parenchymal abnormalities, the incidence of abnormal scans ranging from 23% to 60% (Willi et al, 1980; Wilson-Sharp et al, 1984; Graham et al, 1985) depending on the age of the group studied, although all these studies showed an increasing incidence of liver involvement with increasing age.

Three distinct histological forms of liver involvement are seen in CF: steatosis, focal biliary fibrosis and multilobular cirrhosis. Steatosis (fatty infiltration) is non-specific for CF, occurring in approximately 30% of cases, and is not age-related. It does not progress to focal biliary fibrosis (Roy, 1980). Focal biliary fibrosis is specific for CF, its incidence from post-mortem studies increases with age, occurring in 10% of infants less than 3 months old to approximately 27% in children over 1 year (Oppenheimer & Esterly, 1975b). Approximately 5% of children with focal biliary fibrosis will progress to cirrhosis in the areas of fibrosis with regeneration nodules and ultimately portal venous hypertension (di Sant' Agnese & Blanc, 1956; Roberts, 1962; Kopel, 1972). The incidence of multilobular cirrhosis increases with age, being reported in 5% of children over 12 years (di Sant' Agnese & Davis, 1979) and in 10% of adults over 25 years (Mitchell-Heggs et al, 1976), although it is documented as early as 3 years (Roy et al, 1982).

The incidence of gallbladder abnormalities in CF is high and increases with age from 20% in the 0–5 years group to 60% in 15–20 years group (Warwick & l'Heureux, 1976); abnormalities include microgallbladder (Feigelson et al, 1975; Isenberg et al, 1976) and gallstones (Feigelson et al, 1975; Isenberg et al, 1976; Hubbard et al, 1978; Kawter & Schwachmann, 1979).

Nearly all patients with CF have evidence of pancreatic exocrine dysfunction (di Sant' Agnese & Davis, 1979) and ultrasound changes indicative of fibrosis have recently been reported (Willi et al, 1980; Wilson-Sharp et al, 1984; Graham et al, 1985).

In view of the frequency of abdominal complications in CF, a prospective study was undertaken to assess the usefulness of ultrasound and to correlate the clinical and biochemical abnormalities.

The preliminary results are reported.

PATIENTS AND METHOD

During the period 1983–84, 83 patients with proven CF had 103 abdominal ultrasound scans; 17 patients had multiple scans. The results for the first 76 patients scanned (46 male, 30 female; age range 11 months–18 years) are analysed (Fig. 1). Real-time sector scans were performed, mainly using a 5 mHz probe but occasionally a 3.5 mHz probe for the larger patients. Patients were scanned in the supine, oblique and sitting position as appropriate, and in some cases a drink was given to aid pancreatic visualisation. Most patients were scanned after a 4 h fast; however, some had recently eaten and in these cases, although a normal gallbladder was often visualised, no abnormalities were demonstrated in the non-fasting state. Liver size was assessed subjectively as either normal, large or small. A comment was made on liver texture, paying particular attention to the contour of the free inferior margin, which was assessed as either smooth or irregular; reflectivity of the liver parenchyma was documented in relation to the renal parenchyma, the latter being taken as normal in CF patients (Taylor et al, 1981). Spleen

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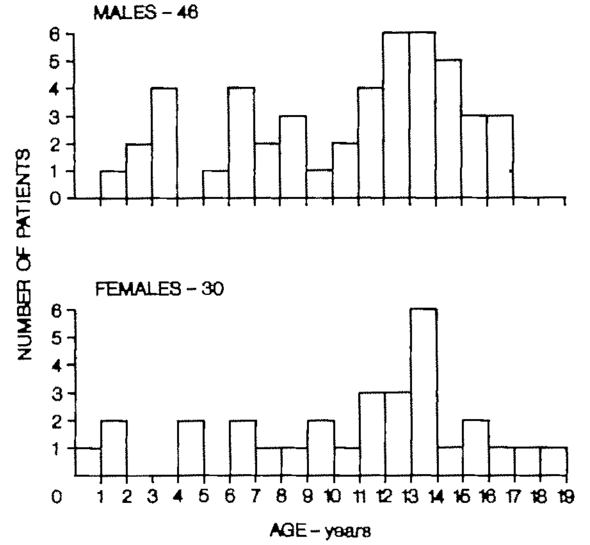


FIG 1

Number and age range of male and female patients.

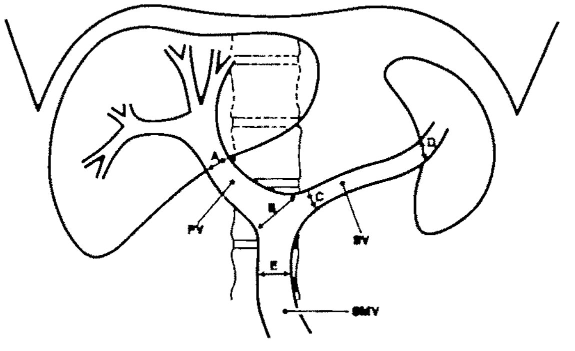


FIG 2.

Site at which measurements were taken. A = PV at the liver hilum, B = confluence of SV and SMV, C = SV at the level of the aorta; D = SV at the splenic hilum; E = SMV, PV = portal vein; SMV = superior mesenteric vein; SV = splenic vein

size was similarly assessed subjectively and again parenchymal texture noted in relation to the left kidney. Portal venous anatomy was imaged as completely as possible and the maximum diameter in full inspiration and expiration were measured, as indicated in Fig. 2. Measurements were taken of the portal vein at the liver hilum and at the confluence of the splenic and superior mesenteric veins; the splenic vein was measured as it crossed the aorta and at the splenic hilum in the supine, transverse or oblique positions, intercostal scans being particularly useful. The diameter of the superior mesenteric vein was recorded from a longitudinal scan. A search for varices was made if the ultrasound findings suggested portal venous hypertension.

The pancreas was examined and reflectivity assessed in relation to the liver at a similar depth, the normal pancreas being just more reflective than normal liver and considerably more than renal cortex (de Graff et al, 1978; Filly & London, 1979). The presence of cysts and calcification was also recorded.

Liver function was considered abnormal if two or more of the following enzyme levels were raised: alkaline phosphatase, alanine transaminase, aspartate aminotransaminase and gamma-glutamyl transpeptidase.

RESULTS

Fifty-six of the 76 patients (74%) had entirely normal liver scans: 20 (26%) were considered abnormal (Table I). The most striking abnormality seen was an irregular edge to the liver (Fig. 3) found in 85% of abnormal scans and in 14 (70%) of these patients the liver function tests were also abnormal. It should be noted that the one patient with a small, smooth liver without splenomegaly had histologically proven renal sarcoid. The two patients with large but smooth-edged livers and without splenomegaly each had additional disease at the time of scanning; one had infectious mononucleosis and the other piperacillin drug sensitivity. The liver parenchyma was homogeneous in all patients and only four patients with small irregular livers, splenomegaly and varices had increased reflectivity.

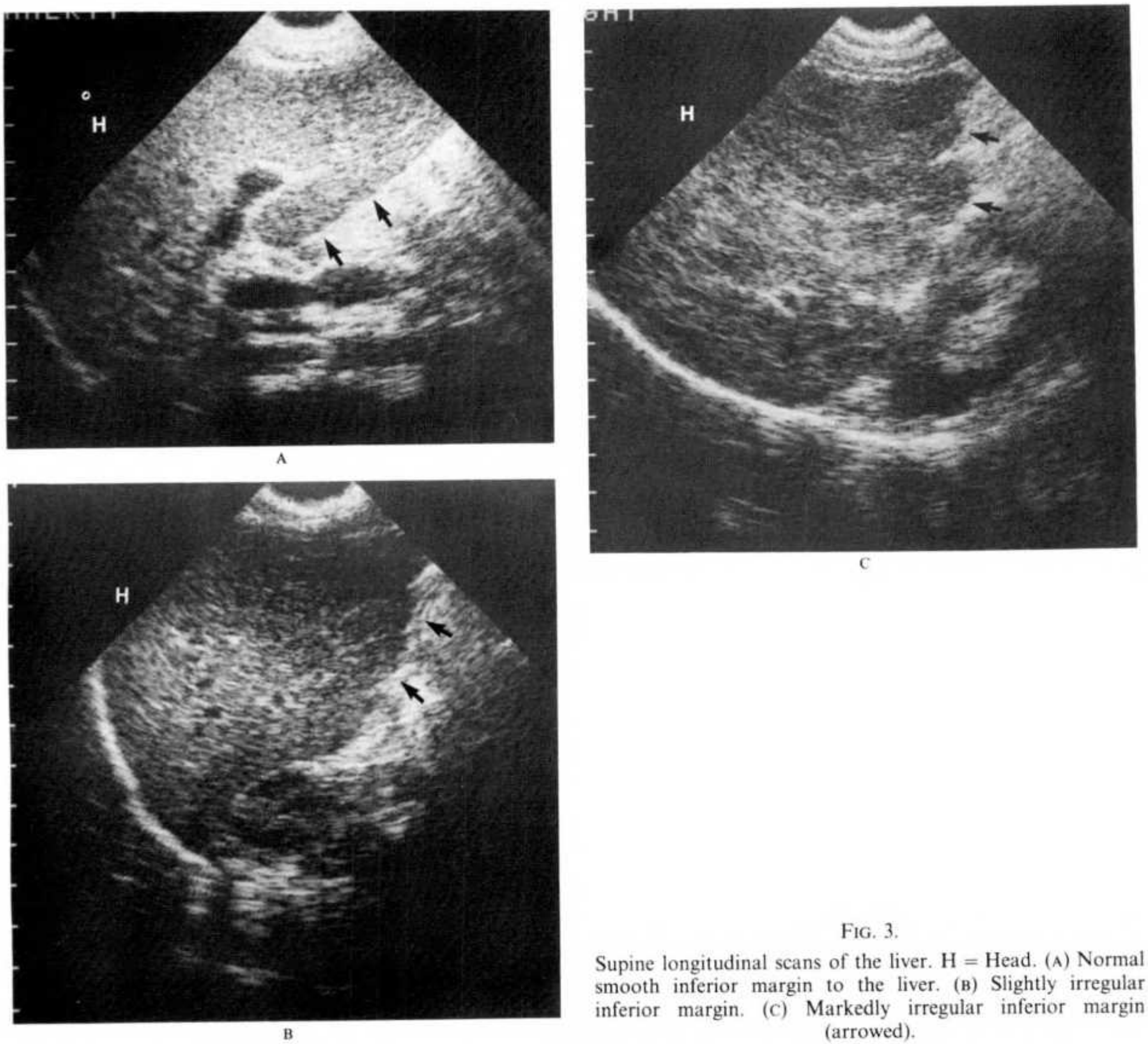
The correlations between the ultrasound findings and liver function tests are shown in Table II. In this series we found no correlation between the absolute size of the portal vein and its tributaries and the ultrasound findings of portal hypertension (splenomegaly and varices); all patients with ultrasound evidence of portal hypertension maintained some variation in the calibre of the portal, superior mesenteric and splenic veins with respiration.

Table III lists the gallbladder and pancreatic ultrasound findings. The gallbladder was normal in 57 (75%), definitely abnormal in three (3.9%) and not visualised adequately in 16 (21.1%) who had not fasted In the three patients with abnormal gallbladder scans, the ultrasound scan had shown a normal liver. The pancreas was considered normal in 24 children (30%), and abnormal with increased reflectivity in 19 (25%).

TABLE I

LIVER ULTRASOUND FINDINGS

Liver size	No.	Irregular edge	Splenomegaly	Varices
Normal	56	0	0	0
Normal	10	10	0	0
Small	5	4	4	4
Large	5	3	1	0



A

B

C

FIG. 3.

Supine longitudinal scans of the liver. H = Head. (A) Normal smooth inferior margin to the liver. (B) Slightly irregular inferior margin. (C) Markedly irregular inferior margin (arrowed).

TABLE II

CORRELATION OF ULTRASOUND FINDINGS AND LIVER FUNCTION TESTS

Ultrasound findings of the liver	Liver function tests (No. of patients)				
	Total No.	Normal	Abnormal	Single abnormal result	Not available
Normal size with an irregular inferior edge	10	1	5	3	1
Small with irregular edge	4	0	4	0	0
Small with smooth edge*	1	1	0	0	0
Large with irregular edge	3	1	1	1	0
Large with smooth edge†	2	0	2		
Normal ultrasound	56	34	3	11	8

*Patient with histologically proven renal sarcoid.

†One patient had infectious mononucleosis and the other had sensitivity reaction to piperacillin.

TABLE III

GALLBLADDER AND PANCREATIC ULTRASOUND FINDINGS

Gallbladder	
Normal	57
Stones	1
Sludge	1
Micro-gallbladder	1
Not visualised (patient non-fasting)	16
Pancreas	
Normal	24
Bright	19
Not visualised adequately	33

The pancreas was not visualised adequately in 33 patients (43%) due to interference by bowel gas.

DISCUSSION

Ultrasound is a safe, non-invasive and relatively inexpensive investigation which is particularly appropriate in paediatrics and its usefulness in assessing abdominal complications is now apparent (Willi et al, 1980; Wilson-Sharp et al, 1984; Graham et al, 1985).

The incidence of pancreatic fibrosis in our study, as evidenced by increased reflectivity, is similar to the experience of Willi et al (1980). However, in a relatively large number of patients (33) it was impossible to examine the pancreas adequately, in spite of fluid distension of the stomach and proximal duodenum, due to the interference of large quantities of bowel gas, an inherent problem in these patients with malabsorption. Small pancreatic cysts are frequently seen post-mortem (Oppenheimer & Esterly, 1975a); in our series no definite pancreatic cysts were seen on ultrasound.

The relatively low incidence of gallbladder abnormalities in this series (3.9%) compared with other studies, where it is cited as high as 60% (Warwick & l'Heureux, 1976) reflects mainly the younger age of our children.

The ultrasound abnormalities of the liver seen in CF have recently been described (Willi et al, 1980; Wilson-Sharp, 1984; Graham et al, 1985) but nodularity of the inferior liver edge has only been briefly mentioned by Willi et al (1980). This was found to be a consistent and quickly assessed abnormality, occurring in 85% of the abnormal liver scans seen in our series.

The ultrasound findings seen in the liver reflect the underlying pathology (steatosis, focal biliary fibrosis and multilobular cirrhosis). Mucinous bile forms plugs which obstruct branch ducts (di Sant' Agnese & Talmo, 1967) and this is followed by proliferation and hyperplasia, resulting in periductal inflammation, fibrosis and eventually focal biliary fibrosis which is CF-specific. Regeneration nodules surrounded by fibrous tissue eventually develop in 5% of these cases. The ultrasound finding of irregularity of the liver edge may precede clinical and biochemical evidence of liver disease. It is thought that the irregularity of the liver edge seen in this study reflects developing hepatic fibrosis. The sensitivity of detecting portal hypertension with ultrasound will probably be increased with combined Doppler and B-mode static scanning when blood flow and velocity as well as anatomy can be assessed.

In view of the number of potential abdominal complications that can occur in CF we feel ultrasound, being a non-invasive investigation, should be part of the routine assessment of these patients.

ACKNOWLEDGMENT

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Book reviews

Recent Advances in Radiology and Medical Imaging (8). Ed by R E Steiner and T. Sherwood, pp x+213, 1986 (Churchill Livingstone, Edinburgh), £45.00
ISBN 0-443-03108-8

As the editors point out, the previous three volumes of this series appeared with only 4 years between them and this current edition has appeared 3 years after the last. Such is the rapid evolution of our specialty. Once again a distinguished group of authors has been assembled and the reader is treated to an excellent selection of review articles.

The first article, by Alexander, reviews both the clinical and radiological aspects of arthritis. This is followed by a description of the features of the chest radiograph in the adult respiratory distress syndrome by Mann and Greenspan. The contribution of computed tomography to the evaluation of disease of the lumbar spine, particularly disc lesions, is emphasised by Dixon. Two chapters follow on magnetic resonance imaging. The first, on the central nervous system by Bydder, reviews the present knowledge and potential of this technique, which is now becoming more widely available Steiner then discusses the potential of the technique in the body and critically analyses its present capabilities and disadvantages. Digital radiographic methods are rapidly developing and Chernin and Capp present digital subtraction extracardiac angiography, while the exciting developments of digital radiography in the chest are presented by Fraser and Barnes. Kirkpatrick gives an overview of modern imaging techniques as applied to paediatric practice and Grainger then allows us to share his wisdom on intravascular contrast media. Examination of the small bowel by barium perfusion techniques is expounded by Nolan. Interventional techniques are then reviewed. angioplasty by Cumberland is followed by a chapter by Kellett, dealing particularly with percutaneous nephrostomy and nephrolithotomy. The last chapter is by Fuchs and Husband, putting into perspective the place of radiology in the staging of malignant disease.

As usual, the standard of these reviews is high, the illustrations clear and adequate and the references comprehensive As the editors point out, there are gaps and indeed there is little on diagnostic ultrasound in this particular volume. However, this gives us the opportunity to look forward to Volume 9, which hopefully will appear at an even shorter interval than its predecessors The editors hope in their preface the series will remain good value They need not worry.

D. G SHAW

Two Dimensional Real Time Ultrasonic Imaging of the Heart. Ed by E R Giuliani, pp 423, 1985 (Martinus Nijhoff, Boston), £82.75.
ISBN 0-89838-671-3

This is a multi-author book of some 423 pages and 37 chapters, each chapter written by a different group of authors There is no uniformity of format, either in the text or in the presentation of the illustrations. Some authors have inverted the images to make them appear more anatomical, *i.e.* with the ventricles at the bottom of the illustrations and the atria at the top The majority have shown them as they come on the echocardiographer's screen, with the atria below the ventricles. The quality of the still frames is also very variable. It would have been interesting to know on which machine each of the scans had been made The reader might then have had a guide either towards or away from specific makes of scanner.

The book starts with an interesting historical account from Edler, the father of echocardiography, on the development of echocardiography from its earliest stages. This is followed by a chapter on the normal heart, which has five pages of double-column text without any illustrations, followed by 10 pages of the illustrations to which the previous text refers. This is an unfortunate opening, as elsewhere in the book the illustrations are scattered evenly through the text It is noticeable how much better the M-mode echoes reproduce than the two-dimensional ones.

The bibliography at the end of each chapter is good, although references from the British literature seem to have been occasionally overlooked.

In general, this is a workman-like book and should be valuable for reference; most of the views are unexceptionable. Some caution might have been included about value of planimetering echoes from the cross-sectional image because of the distortion that is inherent in cross-sectional echocardiography

R B PRIDIE

1987, *The British Journal of Radiology*, *60*, 143–153 FEBRUARY 1987

Accuracy and precision in the measurement of relaxation times from nuclear magnetic resonance images

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ABSTRACT

The accuracy (proximity to the true value) and precision (reproducibility) of relaxation times derived from nuclear magnetic resonance images were investigated. Two methods of deriving relaxation times were considered. (1) A patient scanning protocol in which the minimum number of scans necessary for the calculation (three) were performed. Calculated T_1 and T_2 images were then formed. (2) An animal (cat) protocol in which many more scans were performed. The data were read from the display and fitted by computer to the theoretical curves. The accuracy of the measurements was determined by an empirical method. A series of bottles with different concentrations of $MnCl_2$ and $CuSO_4$ in water were prepared and their relaxation times determined using the imager as a simple pulsed spectrometer. These values were compared with those derived from images. Over the normal range of tissue values ($T_1 < 700$ ms, $T_2 < 200$ ms) the animal protocol gave values of T_1 up to 1% shorter than the true values. The T_2 values were up to 5% shorter. Patient protocol values were up to 7% shorter for T_1 and up to 20% shorter for T_2. There was some difference between results for $MnCl_2$ and for $CuSO_4$ (particularly for patient T_2s), suggesting that the results depend to a small extent on the T_1/T_2 ratio. The precision of the values was investigated by considering the standard deviations (SDs) of brain tissue measurements over populations of cats (animal protocols) and normal control subjects and multiple sclerosis patients (patient protocols). These were compared with the SDs of measurements of calibration bottles scanned with the patients. Standard deviations of 3% for T_1 and 6% for T_2 were found over 19 cats using the animal protocols; SDs of 7% for T_1 and 14% for T_2 were found over 15 normal control subjects using the patient protocols. Standard deviations of bottle measurements were similar to these figures. There are also variations between different subjects and different regions of the brain. There was no significant change between readings on the same patient in follow-up studies. Other sources of variation in the measurements made with the patient protocols were investigated by scanning phantoms. Noise in T_1 and T_2 images is about 2%. Spatial non-uniformity within slices is about 1% for T_1 and 10% for T_2. Non-uniformity between slices in multislice sets is 4% for T_1 and 14% for T_2. There is no long-term variation in measured values over 9 months, short-term variation is ~ 1%.

Magnetic resonance imagers are capable of defining great anatomical detail. There is also the hope that quantitative data (specifically, measurements of spin density and relaxation times) will provide information on pathological processes *in vivo*. The derivation of such information presupposes accurate and precise measurements of these parameters. ("Accuracy" describes the systematic error in a measurement; "precision" describes variation in measurements made on different occasions.) In this paper we discuss some problems that arise in making measurements of the relaxation times, T_1 and T_2, and present results from a particular imager (Picker 0.5 T, software MR4B) used to image the brain. We were particularly concerned to establish that the experimental imaging protocols (used for cats) and clinical imaging protocols yielded precise values of T_1 and T_2. We also wished to establish the accuracy of the values produced by the manufacturer's algorithms. To these ends we have carried out measurements on phantoms, the brains of patients and normal control subjects and the brains of normal cats.

PROTOCOLS

In both the animal and clinical imaging protocols the reconstruction technique was two-dimensional Fourier transform imaging (Edelstein et al, 1980). The T_1 and T_2 weightings were achieved by the use of inversion recovery (IR) and spin-echo (SE) pulse sequences (Young et al, 1982), respectively. The pulse sequences used were based on those provided by the manufacturer of the imager, although modifications were implemented to reduce the field of view from 30 cm to 15 cm for the animal imaging protocols. The sequences were checked to ensure that pulse angles were correct and that gradient rephasing (Sutherland & Hutchison, 1977) was performed correctly. Ninety-degree pulse angles were calibrated by varying pulse amplitude until the maximum signal was observed; 180° pulses were calibrated by minimising signal amplitude. Rephasing was calibrated by varying the amplitude of the rephase gradient (Sutherland & Hutchison, 1977) to maximise the signal. The field of view and pulse timings were also checked for each sequence.

Animal protocols

For the cat work, T_1 and T_2 were determined from several SE and IR single-slice scans. Typically five to 10 SE scans (echo times, TE, ranging from 40–800 ms) and five IR scans (inversion times, TI, ranging from 200 to 700 ms) were used. The repetition time, TR, was kept constant at 2 s. One hundred and twenty-eight values of phase encoding gradient with two signal averages were used, so that a single scan took about 9 min. The resolution volume was approximately 1.2 mm × 0.6 mm × 5 mm. The T_1 and T_2 values are obtained by least-squares fits of theoretical curves (see below) to image intensities measured from the display.

Clinical protocols

A multiple-scan examination is impractical with patients because it can take several hours. Consequently it is desirable to produce T_1 and T_2 values from a restricted examination. Our standard examination sequence consists of the minimum number of scans required to calculate the parameters: two spin-echo sequences and an inversion-recovery sequence. The sequences are chosen to give useful images in their own right, although they are not optimised for this. The timing of the sequences is given in Table I. All the scans are multislice (Crooks et al, 1982) with slice thickness 10 mm (slice centres separated by 12 mm). Using 128 values of phase encoding gradient and two signal averages, the total examination lasts about half an hour. During this time data are collected from eight slices (16 with the $SE_{2000/40}$ scan) so that a block of tissue 9.6 cm thick is examined. The resolution volume is approximately 2.4 mm × 1.2 mm × 10 mm. Calculated T_1 and T_2 images are produced by the manufacturer's algorithms using these three sets of images as input data.

ACCURACY

Redpath (1982) has shown that image response can be predicted theoretically, and that accurate values of T_1 can be obtained from images. However, the validity of the predictions depends on detailed knowledge of the radiofrequency (RF) pulses. Our pulse sequences are more complex (in some cases multislice and therefore employing multiple selective RF pulses) and the information required for detailed theoretical analysis was not readily available. We therefore adopted a simpler, empirical approach to determining the accuracy of relaxation time values obtained from the images. Human and animal protocols were assessed separately since the potential sources of inaccuracy are different in each case.

TABLE I

STANDARD PATIENT EXAMINATION SEQUENCES

Name	Echo time TE (ms)	Inversion time TI (ms)	Repetition time TR (ms)	Comments
$SE_{2000/40}$	40	—	2000	Relatively independent of T_1 and T_2
$SE_{2000/120}$	120	—	2000	T_2-dependent
$IR_{2000/500/40}$	40	500	2000	T_1-dependent

Calibration of standard solutions

A series of solutions of manganese chloride and copper sulphate were made up in small polythene bottles, 5 cm in diameter, filled to a depth of about 5 cm. The T_1s of these solutions ranged from 250 ms to 2 s and the T_2s from 70 ms to 1.5 s. At 0.5 T the relaxation times (in seconds) of a solution of $MnCl_4.4H_2O$ were found empirically to be given, approximately, by the equations

$$1/T_1 \sim 0.4+50c;\ 1/T_2 \sim 0.4+210c$$

where c is the concentration in gl^{-1}. For $CuSO_4.5H_2O$ the corresponding equation was found to be

$$1/T_1 = 1/T_2 \sim 0.4+4c$$

These solutes were chosen since they provide solutions with different T_1/T_2 ratios ($\sim$ 4 for $MnCl_2$, 1 for $CuSO_4$). Ideally a solution with a similar ratio to that of tissue would be used (about 5–6). However, no simple solute which gives such a ratio is available.

We did not have access to a spectrometer operating at the field of the imager to measure the relaxation times of these solutions, so we made use of the imager itself. This was programmed for IR and Carr-Purcell-Meiboom-Gill (CPMG) pulse sequences without gradients (Farrar & Becker, 1971). The signal was measured directly from an oscilloscope connected to the output of the phase-sensitive detector. The signal in each channel was measured and the magnitude calculated. A period of at least $5T_1$ was left between excitations to allow the magnetisation to return to equilibrium. The signal sizes are given by

$$S_{CP} = G\cdot\rho\cdot\exp(-TE/2) \qquad (1)$$

$$S_{IR} = G\cdot\rho\cdot\exp(-TE/2)[1-2\cdot\exp(-TI/T_1)] \qquad (2)$$

where:

S_{CP} is the CPMG signal magnitude;
S_{IR} is the IR signal magnitude;
G is a constant representing system gain;
ρ is the spin density.

T_1 was determined from the IR sequences by altering TI, keeping TE fixed and performing a least-squares computer fit to Equation (2). T_2 was determined by a computer fit of Equation (1) to the CPMG data. The standard errors of these fits were less than 1% for T_1 and 2% for T_2. For the calibration experiments the bottles were placed in the centre of the magnet. They were equilibrated to 22°C (room temperature in the air-conditioned laboratory) in a water bath before the experiments and were never left in the magnet for longer than 10 min. No appreciable temperature rise was noticed over this period.

The homogeneity of our magnet is approximately 5 ppm over a sphere 30 cm in diameter. We would expect the homogeneity over the volume of the calibration bottles to be better than 1 ppm (corresponding to a bandwidth of 20 Hz). The RF pulses were

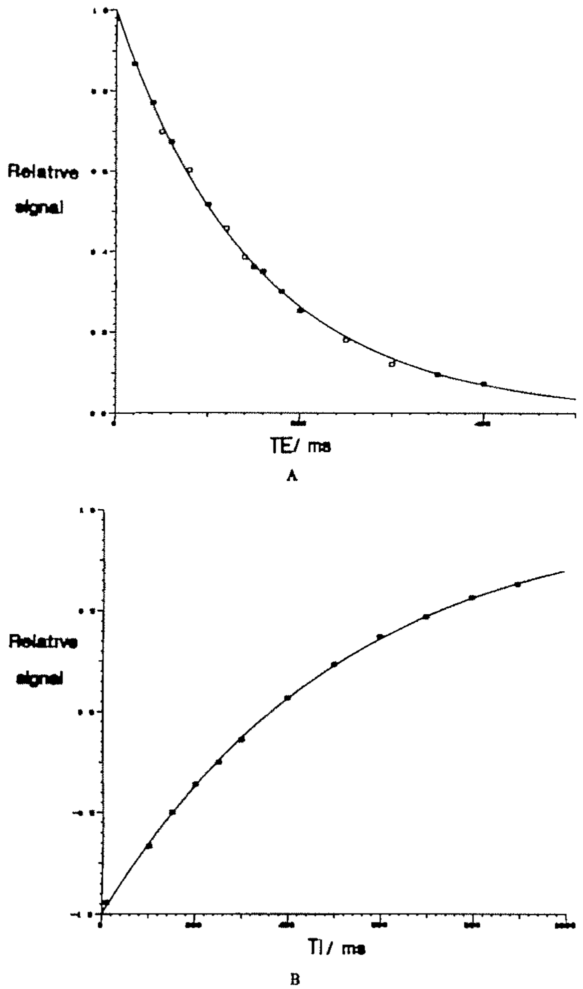

FIG. 1

Fitted curve and experimental points from calibration procedure on a typical solution (A) S_{CP} data, fitted $T_2 = 150$ ms (B) S_{IR} data, fitted $T_1 = 523$ ms.

rectangular and 800 ms long (corresponding to a bandwidth of 1250 Hz). Consequently we would not expect any off-resonance effects (Farrar & Becker, 1971). The quality of the RF pulses was checked by maximising signal after a 90° pulse and minimising after a 180°. The two pulses were calibrated separately as the output of the RF amplifier was found to be non-linear. The standard transmitter coil (diameter ~ 50 cm) and the standard head receiver coil (diameter 30 cm) were used so that RF field uniformity would be good over the bottle

Figure 1 gives plots of the fitted curves against the experimental data for one typical solution. There appear to be no systematic errors resulting from off-resonance or diffusion effects.

This approach to calibrating solutions is not ideal. Errors due to imperfections in the machine (*e.g.* non-linearities in the receiver) may have similar effects in the calibration and imaging procedures. However, the calibration experiment is very different to an imaging experiment (in particular, no gradients are used, the RF pulses are different and the pulse timing is different) and we believe it does give an independent and accurate measurement of relaxation times. The good fit of the experimental results gives us further confidence in this approach.

Animal protocols

The standard solutions were scanned with the sequences used in the animal protocols (see above) and the image intensities read from the displayed image.

The conventional equations used to describe SE and IR image intensities are based on Equations (1) and (2) modified to account for finite repetition times (*e.g.* Ortendahl et al, 1984)

$$I_{SE} = G\cdot\rho\cdot\exp(-\mathrm{TE}/2)\cdot[1-\exp(-\mathrm{TR}/T_1)] \qquad (3)$$

$$I_{IR} = G\cdot\rho\cdot\exp(-\mathrm{TE}/2)\cdot[1-2\exp(-\mathrm{TI}/T_1) + \exp(-\mathrm{TR}/T_1)] \qquad (4)$$

where:

I_{SE} is the SE image intensity, and
I_{IR} is the IR image intensity

(These equations neglect the effects of flow and diffusion.)

These equations are approximations which are only valid under certain conditions. For instance, TE should be much less than TR when T_1 is long (Taylor & Ericsson, 1983) and the flip angles should be correct at all positions in the slice (Redpath, 1982). We wished to test the validity of these approximations for the pulse timings we are using.

A minimum of three scans is needed to solve Equations (3) and (4) (three unknowns). Many more than this were collected (typically 10–15) so that the data are overdetermined and a least-squares fitting program was used to find T_1 and T_2 from the measured image intensities.

The standard error from the computer fit in the T_1 measurement was better than 4% up to T_1 values of 1 s but became considerably worse thereafter (presumably as a result of the inappropriately short TIs that were used). The standard error in the short T_2 measurements was better than 8% but began to deteriorate at values longer than about 200 ms.

Figure 2 gives plots of the fitted curves against the experimental data for one typical solution. There do not appear to be any systematic errors.

Animal protocol values are plotted against calibration values in Fig. 3. In the case of T_1 there is little systematic error below 2 s although most animal protocol values are slightly shorter than the calibration values Animal protocol T_2s are rather less accurate, being about 5% shorter than the calibration values

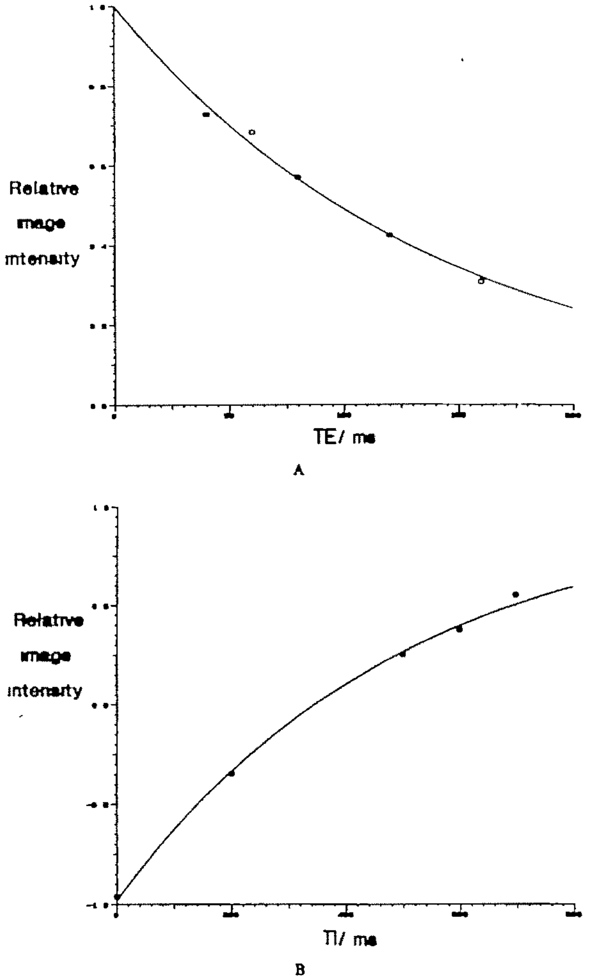

FIG. 2

Fitted curve and measured image intensities for animal protocol images of a typical solution. (The bottle is the same as that of Fig. 1.) (A) I_{SE} data, fitted T_2 = 141 ms. (B) I_{IR} data, fitted T_1 = 510 ms

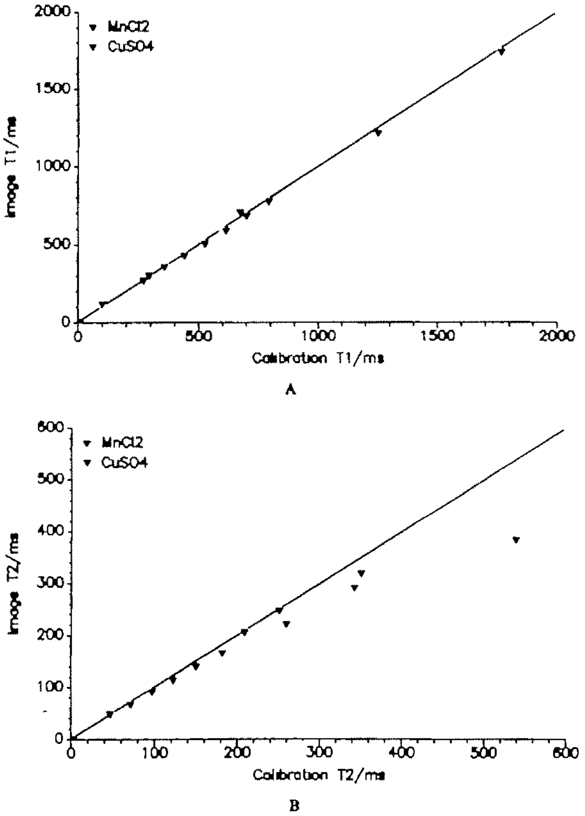

FIG. 3

Plot of relaxation times measured by the animal imaging protocols vs relaxation times measured by the calibration procedure. (A) T_1. (B) T_2.

below about 200 ms. Above about 400 ms the T_2 values are considerably less accurate. There is little difference between results from $CuSO_4$ and $MnCl_2$ solutions, which suggests that these measurements are relatively independent of the ratio of T_1/T_2.

Patient protocols

The standard solutions were scanned using the three sequences used in the patient protocols and the images were used as input data for the formation of calculated T_1 and T_2 images by the standard algorithms. The relaxation times were then read from the calculated images. Measurements could only be taken from a single slice of the eight-slice set because of the size of the bottles (the fifth slice was used). There was some variation from slice to slice, which is discussed below. The T_1 values from Slice 5 are ~ 2% higher than the values averaged over all slices The T_2 values from Slice 5 are ~ 4% low.

Image values are plotted against the calibration values in Fig. 4. There is a systematic error which increases to about 7% at T_1 values of about 700 ms. There is also a 20% error in T_2 values which increases at T_2s of over 200 ms. The image T_2 values of $MnCl_2$ solutions are lower than those of $CuSO_4$ solutions, suggesting that the accuracy of these measurements depends on the ratio of T_1/T_2. The accuracy of tissue measurements may, therefore, be worse than 20%.

Discussion

Diffusion One possible cause of inaccuracy in T_2 measurements is diffusion (Taylor & Bushell, 1985). The self-diffusion of spins in gradients can cause signal attenuation which may mimic T_2 decay. However, the decay curve would become distorted (non-exponential) and there is no evidence of this in the animal data (Fig 2A). To test this further, T_2s were measured using

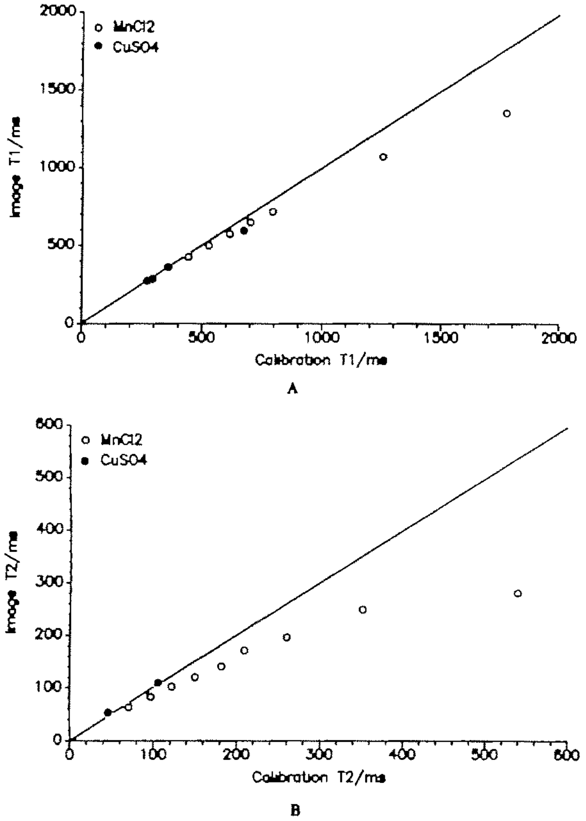

FIG. 4

Plot of relaxation times measured by the patient imaging protocols vs relaxation times measured by the calibration procedure. (A) T_1 (B) T_2

single-slice head and animal protocols. Head scans use weaker gradients than animal scans so, if diffusion has any effect, the measured values of T_2 should be longer in the head images. This was not found to be the case for the standard solutions so is unlikely to be the case for tissue water which has self-diffusion coefficients about half that of pure water (Beall et al, 1984).

Multi-exponential decays. A fundamental limitation of the limited scan protocols used for patients is that they are incapable of detecting multiple exponential behaviour There is evidence that most normal tissues (including brain tissues) exhibit multi-exponential T_1 and T_2 decays (Bakker & Vriend, 1984; Parrish et al, 1974). However, it is usually the case that at least one component is much shorter than the shortest value of TE used (40 ms) Consequently this component will have decayed before the signal is collected and will not be detected. The T_2 components which are much longer than the difference between the two TEs (40 ms and 120 ms) will also be undetectable since the amount of decay between the two readings will be small. The accuracy of the measurements may not then be greatly affected although they would only represent a single, dominant component.

Using these animal protocols we were unable to detect multi-exponential behaviour in normal feline grey and white matter, but only in cytotoxic and severe vasogenic cerebral oedema (Barnes et al, 1986).*

Inadequacy of the model. The inaccuracy in the relaxation time measurements is probably due to the approximations involved in Equations (3) and (4). In particular, the effective flip angle for selective 90° pulses may be much less than 90° for long-T_1 solutions (Redpath, 1982). The use of selective 180° pulses (for multislice scans) introduces further complications. Moreover, it will almost certainly be the case that the profile of the inverted slice (180° flip) and the excited slice (90° flip) will not be identical, although what effect this has on relaxation time measurements still needs to be elucidated. The approximation that TE should be much shorter than TR does not hold for the very long TEs (800 ms) that are sometimes used. It is possible to correct for this by saturating the spins after signal collection (Tofts et al, unpublished). Alternatively a Carr-Purcell sequence can be used.

It is also assumed that the different image sequences are properly set up, *e.g.* that the field of view is constant and that the magnetisation is rephased correctly (Sutherland & Hutchison, 1977) in all the scan sequences. However, this assumption may be incorrect. We have noticed that particular SE sequences can give consistently low or high readings as a result of incorrect calibration. Uncorrected gradient eddy currents, particularly in multislice scans, may also cause inaccuracy.

PRECISION

In making estimates of the precision of relaxation time measurements it is possible to distinguish three causes of variability in measurements. Firstly, there are variations which are attributable to imperfections in the machine (some of which are unavoidable). Secondly, some variation may be caused by the inhomogeneous nature of the subject (patient) and consequent partial-volume effects. Finally, there may be variations which reflect real tissue differences and consequently are not causes of imprecision at all The different causes of variation have been investigated by serial and parallel studies of phantoms and the brains of normal control subjects (including cats) and multiple sclerosis patients. Calibration bottles of $MnCl_2$ solutions were included in all scans; however, the temperature of these bottles was not stabilised. Although the NMR unit is air-conditioned and has very stable temperatures, the bore of the magnet is 2–3 K colder. The relaxation times of $MnCl_2$ solutions are less sensitive to temperature changes than $CuSO_4$ solutions (Hausser & Noack,

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*Subsequent improvements in accuracy have allowed the detection of bi-exponential behaviour in normal feline white matter (Barnes, unpublished results).

1964) but still vary by ~ 1% per K. Consequently much of the variability in measurements on these bottles can be attributed to temperature variation. There is unlikely to be a similar effect in tissue due to the stability of body temperature. Further variation is introduced into bottle measurements made with the animal protocols by the non-uniform response of the receiver coil. The calibration bottle was at the edge of the field of view, where small changes in the position from which the measurement is taken can introduce large changes in image intensity.

Imager imperfections

There is a variety of imager imperfections which might cause imprecision in relaxation time measurements.

(i) *Image noise* is always present and will introduce inevitable imprecision in relaxation time measurements.

(ii) *Temporal instability*, both short-term (during a single examination) and long-term (between examinations), will cause imprecision.

(iii) *Image non-uniformity* will cause imprecision if the measured volume of tissue is not always in the same place in the imager.

(iv) *Interactions between patient and imager*. These can include attenuation of the RF pulse as it penetrates tissue and damping of the transmitter coil (resulting in pulse-angle errors). Since these effects depend on the volume and nature of the patient they can introduce further imprecision.

(v) *Sequence dependence*. Relaxation times may depend on the details of the sequences used for their derivation. For instance multislice and single-slice protocols will almost certainly give different values since the slice profiles will be different. If all sequences are not calibrated correctly (*e.g.* for magnetisation rephasing (Sutherland & Hutchison, 1977)), calculated values of relaxation times will depend on which sequences are used.

Strictly speaking, (iii)–(v) are causes of inaccuracy rather than imprecision, since they give a systematic error for a given set of imaging circumstances. However, since these circumstances are not usually reproduced exactly from one examination to the next, we are considering them under the heading of precision.

Noise was defined as the standard deviation of the relaxation time measurement divided by the mean. For the patient protocols this was estimated directly from readings from frontal white matter (where partial-volume effects should be small) and calibration bottles. The noise in T_1 was ~ 1% for white matter and the bottle. The noise in T_2 was ~ 2% for white matter and ~ 4% for the bottle. However, most of the variation in the bottle measurements is due to ringing artefacts caused by the sharp edges of the bottle image. The variations in tissue measurements caused by noise depend on the number of pixels over which the measurement is averaged. This is generally between one and 40, depending on the extent of the measured tissue. Noise in the animal protocol values is less easy to estimate since it depends on the number of sequences used, their timing and the weighting they are given in the fit. However, thermal noise in a typical spin-echo image used in the animal protocol (TE = 80 ms, TR = 2000 ms) is ~ 3%.

Phantoms were scanned repeatedly to estimate short-term variability in individual scans. In individual scans there was less than a 1% variation in image intensity over a single day. This might introduce a somewhat greater error into calculated relaxation times.

There were no significant differences between mean results obtained from the calibration bottles at the beginning and end of a 9-month period. There were day-to-day variations of 6–8% (standard deviation) in the measurements (see Tables IV and V) which are partly due to temperature fluctuations.

Image non-uniformity was investigated by scanning uniform phantoms. Non-uniformity of the images produced under the animal protocols is dominated by the non-uniform response of the closely coupled receiver coil used. This introduces a constant factor into each of the sequences used in the calculations. Consequently the relaxation measurements are independent of position, provided the readings are taken from the same area in each scan. However, in peripheral areas where image intensity is changing rapidly with position, a small positioning error can cause a large error in the measured intensity. But image intensity is quite uniform over the brain of the cats, so receiver coil inhomogeneity is unlikely to be a problem. Moreover, care was taken to ensure that the cats were always in the same position relative to the coil and that the coil was always in the same position within the bore of the magnet.

In the multislice sequences used in the patient protocols there are additional non-uniformities introduced by uncorrected eddy currents distorting the gradient field. These introduce non-uniformities from one slice to the next and also within a single slice. Since this effect is sequence-dependent (unlike the non-uniform response of the receiver coil), it can introduce non-uniformities in the images of calculated relaxation times. Slice-to-slice non-uniformity occurs because eddy currents build up during the multislice sequence and progressively alter slice width. This is illustrated in Fig. 5, which is a plot of image intensity (for a single position within the slice) versus slice number for two eight-slice sequences similar to those used for the T_1 calculation. The findings can largely be explained as the result of eddy currents producing gradients in the slice select direction. A gradient in this direction will tend to reduce slice thickness and hence reduce image intensity, although the magnitude of the effect is difficult to predict when multiple selective RF pulses are used. The order in which the slices are sampled in each case is $1–t_1–3–t_1–5–t_1–7–t_2–2–t_1–4–t_1–6–t_1–8–t_3$, where t_n gives the interval between sampling (For $SE_{2000/40}$, t_1 ~ 100 ms, t_2 ~ 100 ms, t_3 ~ 1200 ms). Consequently, as

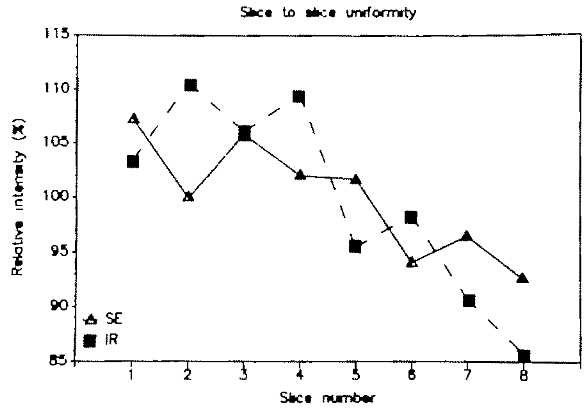

FIG. 5

Plot of image intensity vs slice number for eight-slice multislice sets ($SE_{2000/40}$ and $IR_{2000/500/40}$)

Slices 1, 3, 5 and 7 are sampled in the $SE_{2000/40}$ sequence, eddy currents build up which reduce signal intensity. The fall in signal intensity continues from Slice 2 to Slice 8. The eddy currents die away almost completely during the relatively long interval t_3. This does not explain all the observations—in particular, image intensity appears to be rising through Slices 7, 2 and 4. However, it does explain the main observation of alternate high and low intensities and the overall tendency of intensity to drop with slice number. The alternation of high and low intensities is reversed for the IR sequence because then the interval t_3 is shorter than t_2 ($t_1 \sim 100$ ms, $t_2 \sim 600$ ms, $t_3 \sim 300$ ms).

Non-uniformity was estimated by taking six relaxation time readings from each slice of a multislice set. The following means were then calculated: (1) a slice mean (over all positions) for each slice, (2) a position mean (over all slices) for each position and (3) a grand mean over all positions and all slices. Within-slice non-uniformity was taken as the maximum deviation of a position mean from the grand mean. Similarly the slice-to-slice non-uniformity was taken as the maximum deviation of a slice mean from the grand mean. Within-slice non-uniformity was better than 1% for T_1 (mostly a left–right difference) and 3% for T_2. Slice-to-slice non-uniformity was 4% for T_1 and 14% for T_2. In estimating non-uniformity the worst combination of slices (*i.e.* Slice 1 with Slice 1 for T_1, Slice 1 with Slice 2 for T_2) was used for the calculations.

The non-uniformity figures will also include the effects of RF transmitter field non-uniformity. However, the dimensions of the transmitter coil are much larger than the field of view so these effects are likely to be negligible. This was confirmed for the central axial plane of the imager by scanning a thin uniform phantom (without a slice selection gradient) with the normal RF pulses and with composite pulses. A 90° $[x]-90°$ $[y]$ composite pulse was used for the 90° pulse (Freeman et al, 1980) and a 90° $[x]-180°$ $[y]-90°$ $[x]$ composite pulse was used for the 180° pulse (Levitt, 1982) where the letters in square brackets refer to the axes about which the rotations occur (*i.e.* the phases of the exciting RF pulses). These composite pulses are much more tolerant of transmitter field non-uniformities However, no differences in the uniformity of the image were seen. The RF field non-uniformity is likely to be even less of a problem in the other planes because of the length of the transmitter coil.

Patient loading of the transmitter coil may reduce flip angles. We have found experimentally that an increase in RF amplitude of about 25% is needed to compensate for this when scanning heads. (This was found by adjusting the amplitude of a 180° pulse to give a signal minimum.) However, this effect is about the same in all patients (except very large ones), *i.e.* unlikely to cause much patient–patient variation. It is advisable, however, to correct for this effect by adjusting RF amplitude for each patient. (This is also necessary to maintain the accuracy of the measurements.)

The RF attenuation in tissue may cause reductions in flip angles in deep tissues. Theoretical attempts to estimate the magnitude of this effect based on uniform tissue models (Bottomley & Andrew, 1978) fail to account for observed behaviour. This effect should increase with operating frequency but no significant RF attenuation has been discovered at operating frequencies three times our own (Bottomley et al, 1984). However, in comparing relaxation times from different tissues, it would be better to compare tissues at similar depths. Cats, being so small, are unlikely to cause appreciable attenuation.

Our patient protocols involve three standard sequences which are never varied. Consequently missetting the sequences will only lead to inaccuracy rather than imprecision. However, if results from different sequences are to be compared, extra care must be taken to ensure that the calibration of the different sequences is identical. This may cause some small variations in relaxation times measured with the animal protocols since there is some flexibility in the choice of imaging sequences

The results of our investigations into machine-induced variations are summarised in Tables II and III.

Tissue inhomogeneity

(i) Partial-volume effects. There is sometimes considerable difficulty in finding a uniform region of tissue

TABLE II

VARIATIONS DUE TO IMAGER IMPERFECTIONS. ANIMAL PROTOCOLS

	T_1	T_2
Long-term temporal instability (over 9 months)	Not significant	
Short-term temporal instability (over 1 day)	1%	1%
Within-slice non-uniformity	Negligible	

TABLE III

VARIATIONS DUE TO IMAGER IMPERFECTIONS: PATIENT PROTOCOLS

	T_1	T_2
Noise	< 1%	< 2%
Long-term temporal instability (over 9 months)	Not significant	
Short-term temporal instability (over 1 day)	1%	1%
Within-slice non-uniformity	1%	3%
Slice–slice non-uniformity	4%	14%

from which to take measurements. This is particularly difficult with the rather thick slices (*e.g.* 10 mm) that are currently used in NMR imaging.

(ii) Repositioning. If measurements are to be taken from patients in follow-up studies, poor repositioning may cause imprecision. This will be particularly true when there are serious partial-volume effects and/or the tissue is particularly inhomogeneous (*e.g.* a tumour).

The difficulty that is most apparent when attempting to take readings from a displayed image is in identifying a uniform volume of tissue. Tissue measurement variations (preferably in serial studies to eliminate differences between subjects) should be compared with variations in bottle measurements to estimate additional imprecision introduced by partial-volume effects. We are not able to draw any firm conclusions from our measurements due to temperature fluctuations affecting our bottle measurements. However, the good long-term and short-term stability of our imager suggests that medium-term (*i.e.* from one examination to the next) instability will not be severe.

The relaxation times of one cat's brain have been measured eight times over a period of 10 weeks. These data are summarised in Table IV. The standard deviation of measurements was less than 4% for T_1 and 3% for T_2. The standard deviation of bottle measurements (6% for both T_1 and T_2) is greater than that of tissue measurements, suggesting that real changes in the bottles' relaxation time (due to temperature fluctuations) have occurred. Furthermore, the tissue variation is less than the standard errors of the fits to the bottle image data obtained in the calibration procedure. This suggests that the figures for the standard error are dominated by miscalibration which is a fixed effect (dependent on echo time) and will not vary from one examination to the next (*i.e* it will not cause variations in serial studies).

TABLE IV

RELAXATION TIMES OF CEREBRAL TISSUE IN NORMAL CATS

	T_1 (ms)		T_2 (ms)	
	Mean ± SD	Range	Mean ± SD	Range
Parallel (19 cats)				
White matter	476 ± 16	426–493	80 ± 5	74–90
Grey matter	618 ± 21	553–640	84 ± 5	75–99
Bottle	638 ± 38	580–661	154 ± 9	123–176
Serial (1 cat)				
White matter	478 ± 18	452–497	87 ± 3	79–93
Grey matter	612 ± 14	589–637	90 ± 3	80–94

TABLE V

RELAXATION TIMES OF CEREBRAL TISSUE IN 15 NORMAL CONTROL SUBJECTS, AGE RANGE 18–60, MEAN 42 YEARS

	No. of samples	T_1 (ms)		T_2 (ms)	
		Mean ± SD	Range	Mean ± SD	Range
Cerebral white matter					
Temporal	26	400 ± 19	349–427	87 ± 9	71–106
Occipital	30	396 ± 22	346–450	85 ± 8	71–106
Frontal	30	376 ± 18	339–400	85 ± 8	70–97
Parietal	28	400 ± 17	357–439	90 ± 11	75–112
Cerebral grey matter					
Temporal	22	608 ± 36	547–667	103 ± 13	87–133
Occipital	22	575 ± 30	526–642	99 ± 9	86–121
Frontal	22	604 ± 42	552–696	112 ± 15	79–133
Parietal	18	588 ± 31	522–638	103 ± 16	84–127
Calibration bottle		442 ± 27		123 ± 10	

The relaxation times of brain tissue in a group of 15 normal control subjects were measured over 6 months (see Table V). The standard deviations of patient values are better than 7% for T_1 and 14% for T_2.

Patient repositioning

If we are to follow the evolution of the relaxation times of a lesion precisely it is desirable to reposition the patient in the same place in follow-up studies. Moreover, the use of some standard position is undesirable since not all patients may be able to maintain that position over the long examination period We have developed a simple means of achieving accurate repositioning of the head. The imager has an alignment system consisting of three lasers which cast narrow lines of light when intersecting a plane perpendicular to the direction of the beam. One shines vertically down on the patient from above and is normally aligned so that it casts a line along the long axis of the patient. This line acts as a sagittal marker. The other two shine horizontally from either side and normally cast lines perpendicular to the long axis of the patient. These lines act as transverse markers. All the laser beams can be rotated about the direction in which the light is emitted so rotating the illuminated line. We have attached a scale to one of the horizontal lasers so that we can measure the angle of rotation.

The alignment procedure is as follows The patient is asked to lie supine with the radiographic baseline as near vertical as possible, but not so as to make the patient uncomfortable. (The radiographic baseline is a line joining the outer canthus of the eye to the inferior border of the external auditory meatus.) For the majority of patients this position will mean a head extension of between 5° and 20°. The patient is adjusted so that the sagittal marker falls on the mid-sagittal plane The transverse markers are used to position the patient so that the interpupillary line is parallel to the transverse image plane. The couch is then positioned so that the transverse markers fall on the lower borders of the external auditory meatuses. The angle that the radiographic baseline makes with the vertical is then measured using the rotating laser with the scale. This angle is the head extension, which is noted. Finally the couch is moved so that one of the transverse markers falls on the outer canthus of the eye, this being the anatomical landmark from which the transverse images can be located. With practice the whole procedure takes less than a minute, and it is straightforward to reposition the patient at any subsequent examination. As a check, the angle of a line between the lowermost point of the clivus and the nasion is measured in the sagittal scout image. We have always achieved repositioning to better than 4° (standard deviation 2°) using this method.

Tissue differences

(i) Patient–patient. There may be variations between different individuals due to race, sex, age, etc.

TABLE VI

ANOVA OF FRONTAL WHITE MATTER MEASUREMENTS OF T_1 IN FOLLOW-UP EXAMINATIONS OF SEVEN MULTIPLE SCLEROSIS PATIENTS

Source of variation	Sum of squares	Degrees of freedom	Mean square	Significance (p value)
Patient	15 971	6	2262	0.012
Examination	16	1	16	NS
Patient × examination	1884	6	314	NS
Residual	25 953	32	811	

(ii) Topographical. There may be differences in apparently identical tissue in different locations in the body (*e.g.* white matter in different lobes of the brain).

(iii) Normal physiological. There are variations in water balance diurnally and with the menstrual cycle and hence possible variations in relaxation times.

(iv) Pathological. Alcoholic intoxication can effect relaxation times (Mander et al, 1985). The relaxation times of diseased tissue may also be abnormal, even when there is no obvious change (see below).

The relaxation times of brain tissue in 19 normal cats have been measured over 9 months (Table IV). The standard deviations of T_1 measurements in the parallel studies was about the same as that in the serial study (less than 4%). The standard deviation of T_2 measurements was about 6% in the parallel and about 3% in the serial studies. These results suggest that the variation between cats is not great.

The relaxation times of apparently unaffected brain tissue were measured in follow-up studies on seven patients with multiple sclerosis. Analysis of variance (Box et al, 1978) was performed on frontal white matter measurements taken from different patients and on different occasions (Table VI). There was no significant variation between measurements made on different occasions; however, there was a significant difference between individuals ($p = 0.012$) although this may be due to the disease affecting the patients to different extents

TABLE VII

ANOVA OF FRONTAL VS OCCIPITAL WHITE MATTER MEASUREMENTS OF T_1 IN TWO HEMISPHERES OF 15 NORMAL CONTROLS

Source of variation	Sum of squares	Degrees of freedom	Mean square	Significance (p value)
Hemisphere	2884	1	2884	0.006*
Lobe	6040	1	6040	< 0.001
Hemisphere × lobe	38	1	38	NS
Residual	19 786	56	353	

*Explained by spatial non-uniformity of images

TABLE VIII

ANOVA OF MEASUREMENTS OF T_1 IN 24 MULTIPLE SCLEROSIS PATIENTS AND 15 NORMAL CONTROLS (FRONTAL WHITE MATTER ONLY)

Source of variation	Sum of squares	Degrees of freedom	Mean square	Significance (p value)
Multiple sclerosis or control	11 691	1	11 691	< 0.001
Residual	23 046	42	585	

Frontal and occipital white matter values were compared in the 15 normal, control subjects (Table VII). These regions were chosen because they are easy to measure (there are large expanses of uniform tissue), they are at the same depth in the head (similar RF attenuation), and they occur in the same slice of a multislice set of images (no slice-to-slice differences). Only measurements from the same hemisphere were compared, to reduce the effects of within-slice non-uniformity. Analysis of variance revealed that the T_1 of frontal white matter is significantly shorter than that of occipital white matter. There is a slight anterior-posterior non-uniformity in T_1 measurements; however, if this were corrected for, it would tend to *increase* the difference. A possible explanation for the variation is that there are differences in the difficulty of finding a uniform volume of tissue from which to take the measurements. In the temporal and parietal lobes the difficulties in finding a large uniform volume of tissue mean that it is much more likely that the measured volume will contain some grey matter or cerebrospinal fluid, and therefore give a slightly longer T_1. However, the difficulty is not great in the frontal and occipital lobes. Moreover, if the measured volume was being corrupted by other tissues we would expect the standard deviation of the measurements to be higher. But the standard deviation is similar in all lobes (although we have not measured the significance of this). We therefore conclude that our measurements show a real difference between frontal and occipital white matter.

We have also compared the relaxation times of apparently unaffected white matter in multiple sclerosis patients with those of the normal controls and found them to be significantly elevated (Table VIII). This may reflect the changes in water balance that are known to occur (Tourtellotte & Parker, 1968). This change also appears to obliterate the difference between the measured T_1s in the frontal and occipital lobes of the normal controls

Discussion

The precision of the tissue measurements is at least approaching that of the bottle measurements, suggesting that partial-volume problems are not as severe as might be feared. The situation would be further improved with narrower slices. It is also clear from repeated scans that apparent imprecision may actually be due to mis-settings of the sequence: a particular data point may fall below a decay curve, not because of noise but because, for instance, the sequence gradients have not been correctly set up. The remaining imprecision will be due to signal-noise and machine instability Artefacts may also cause imprecision: NMR images are prone to ghosting and blurring in the direction of the phase-encoding gradient if any changes (*e.g.*, movement) occur during the course of the scan. It is also important that the images from which calculated T_1 and T_2 images are produced coincide spatially, otherwise there are spurious borders where values have been calculated from readings from two different tissues.

CONCLUSIONS

Relaxation times derived from the animal protocols are accurate to 1% for T_1 and 5% for T_2 over the range we have found in most normal and pathological tissues ($T_1 < 1$ s, $T_2 < 200$ ms). However, some oedematous tissues can have very long T_2 components (Barnes et al, 1986) and the measurements of these will be considerably less accurate. The precision (standard deviation) over the normal range is better than 6%.

Relaxation times derived from the patient protocols are accurate to 7% and 20% (T_1 and T_2, respectively) over the range found in most normal and pathological tissues ($T_1 < 700$ ms, $T_2 < 200$ ms) although some acute demyelinating lesions can have T_1s longer than 1 s. The precision (standard deviation) over the normal range is better than 6% for T_1 and 8% for T_2.

Multipoint calculations (from the animal protocols) give more safeguards against the inaccuracy that results when some of the scan sequences have been set up incorrectly. However, this is no substitute for checking that the scan sequences have been correctly set up. The decreased accuracy of values derived from the patient protocols can probably be ascribed to the difficulties associated with multiple selective RF pulses and increased eddy currents rather than the limited number of data points.

The precision of two-point calculations (from the patient protocols) will be less than that of multipoint calculations because fewer readings are taken. However, with sufficient care, precise measurements can be made on normal tissue from pairs of images. It is dangerous to extrapolate from the precision that can be achieved with normal tissue to that which can be achieved with lesions since the extent and homogeneity of the latter are not so well defined. But provided care is taken to minimise partial-volume effects (and this may mean using narrower slices than is common at the moment) we believe equal precision can be achieved on measurements of lesions.

It is important to know the accuracy of relaxation time measurements so that valid comparisons can be made between different imagers (operating at the same field). It is also important to know the precision of the measurements since this allows us to tell whether the relaxation time differences that are measured are real. Our results suggest that the wide spread in measured values is due to real variations and not a lack of precision. Furthermore, in carrying out calibration work it is possible to discover imperfections in the imager. Correcting these not only improves the accuracy and precision of the measurements, but can also improve the quality of the images. It is certainly the case that the accuracy of our measurements has improved as a result of this investigation.

NOTE ADDED IN PROOF

Since this investigation was performed eddy-current correction has been improved by hardware pre-emphasis of the gradient waveforms Patient-protocol T_1s now show no systematic error and T_2s are only 4% shorter than calibration values over the clinical range Uniformity in the calculated images is now less than 2% for both T_1 and T_2. Variation in cerebral white matter values over control groups has been reduced to 3% and 6% for T_1 and T_2, respectively.

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Book reviews

An Introduction to Biomedical Nuclear Magnetic Resonance. Ed by S. B. Peterson, R. N. Muller and P A Rinck, pp viii + 190 + index, 1985 (Georg Thieme Verlag, Stuttgart), DM120 (£48 00).
ISBN 3–13–669401–5

Intended for the serious student requiring a good basic overview of magnetic resonance, this multi-author text is based, in part, on meetings of the European Workshop in NMR in Medicine, 1983–85. It is divided into three main sections describing the physical principles of both magnetic resonance imaging (MRI) and spectroscopy (MRS), followed by a discussion of the components that make up a magnetic resonance image and concluding with clinical applications to imaging and spectroscopy.

The physics of magnetic resonance is well presented, with many useful diagrams and simple analogies given. The rationale for measurement of relaxation times from multiple data points is discussed. There is a short chapter relating to the safety aspects for patients and personnel. Section 2 deals with the complex interrelationship of tissue and machine (operator) parameters The clinical relevance of "computed", as opposed to "weighted", images is mentioned. There follows a detailed exposition on magnetic resonance flow imaging, concluding with a short addendum to include more recent publications (from 1985) The early clinical research into the applications of magnetic resonance is then presented in the final section. There are separate chapters on the central nervous system, spine, cardiovascular system and abdomen. In the cardiovascular system the work of two groups, from Boston and San Francisco, is presented. Various potential oncological uses are described in a separate chapter Finally, there is a balanced introduction into the feasibility and problems relating to MRS. A comprehensive bibliography (up to 1984) is given at the end of each chapter. There is a useful glossary and a short index.

The purpose of this book is to give the reader a basic knowledge, in order for him to pursue magnetic resonance studies on his own. It goes a long way in achieving this goal. There is a wide range of topics covered and the subject matter is well organised. Inevitably, with multi-author collaboration, there is variation in literary style between chapters, but the editors are to be congratulated in reducing much duplication and providing a readable text. The clinical application section reflects early results, but does provide a basis on which to assess current work. Scant mention is made of the application of MRI in the pelvis or musculoskeletal system, or of the use of paramagnetic tracers. This is to be expected, however, in view of the rapid development that has occurred over the last 2 years

The book is a useful and interesting summary of the work of many of the pioneers in magnetic resonance, and is good value. All MRI departments should have one

J. P R. Jenkins

Magnetic Resonance Annual 1986. Ed. by Herbert Y. Kressel, pp. xii + 267, 1986 (Raven Press, New York), $64.00.
ISBN 0–88167–155–X

This annual is intended for both radiologists and physicists, especially those working in the field of magnetic resonance imaging (MRI). This well presented book contains very good articles on MRI of the spine, central nervous system, musculoskeletal system, chest, breast and liver. More up to date materials are discussed in the chapters on high-resolution MRI using surface coils and magnetic resonance chemical shift imaging. Although these two chapters are rather technical, that on chemical shift imaging is particularly useful, so much so that the idea of the phase contrast imaging was adapted on to our MRI scanner.

The chapter on magnetic resonance spectroscopy, although interesting, is more beneficial for those working at centres with magnets of such capability. The final chapter summarises the effects and explains its basic, underlying mechanisms. It will be helpful to those who are struggling to understand the subject

However, as the paramagnetic contrast agent gadolinium DTPA has been used experimentally for nearly 2 years, it would have been nice to have an article on its clinical application. Perhaps this will be covered in the 1987 edition.

On the whole, the book is very well written and is a must for beginners, and it is also valuable to those who are already in the field. The price of $64 is definitely good value for money.

A W L Leung

1987, *The British Journal of Radiology*, 60, 155–165 FEBRUARY 1987

Patient doses and risks from diagnostic radiology in North-east Italy

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ABSTRACT

A study has been conducted to assess the impact of radiological practice in 1983 in Friuli-Venezia Giulia, a region of North-east Italy with 1 250 000 inhabitants. The design involved three phases: (i) a regionwide frequency survey; (ii) dosimetric measurements on patients in all public X-ray facilities; (iii) derivation of organ doses from those measurements. Frequencies by type, age and sex and values of the main technical parameters of radiological examinations are presented. Organ doses, effective dose equivalents and risk estimates are given for 14 selected examinations. The annual per-capita effective dose equivalent and the genetically significant dose are estimated at 0.848 mSv and 0.253 mSv, respectively. From these values, collective risks have been predicted by using the risk factors given in the International Commission on Radiological Protection Publication 26. The results indicate that 14 persons risk induced malignancies and 2.5 persons risk genetic detriment.

In 1977 the International Commission on Radiological Protection (ICRP) issued new recommendations on radiation protection (ICRP, 1977) and laid down a system of dose limitation to implement these recommendations, which included three elements: the justification of the practice, the optimisation of radiation protection, and the limits of individual dose equivalent. The application of these concepts to patient protection in medical radiology was then detailed in ICRP Publications 33 and 34 (ICRP, 1982a, 1982b). The present work is concerned with the first two elements of the system of dose limitation. It aims to provide a sufficiently accurate database to evaluate both the individual and collective impact of medical radiological practice in Friuli-Venezia Giulia (FVG), a region of North-east Italy with 1 250 000 inhabitants. Furthermore, these data may provide information to justify particular practices, to assess the health detriment to the population due to medical radiation, and to identify both the types of examinations where dose reduction is reasonably achievable and the methods to accomplish it without impairment of diagnostic value. At present, no exhaustive information is available on the current level of diagnostic exposure in Italy. Only a tentative estimate of the genetically significant dose was made in 1974 (Benassai et al, 1977) on the basis of film consumption and doses recorded in the literature.

This is the first estimate of frequencies, individual and collective doses and associated risks of radiographic examinations in Italy. The results can be properly compared with those of the National Radiological Protection Board (NRPB) in Great Britain and the Centre d'Etude sur l'Evaluation de la Protection dans le Domaine Nucleaire (CEPN) in France, since common dosimetric methods were adopted.

In this work the frequencies, the age and sex distributions, and the main technical parameters of radiological examinations have been determined by a statistical survey in all the X-ray departments and offices of the region. Entrance skin doses, as well as doses to superficial organs of interest, were measured directly with thermoluminescent dosemeters (TLDs) in a sample of patients undergoing 14 selected examinations. Entrance doses were converted to organ doses using Monte Carlo conversion factors calculated at the NRPB (Jones & Wall, 1985). The effective dose equivalent was calculated for each of the selected examinations. The frequency and organ-dose data were combined to derive two indices of the collective detriment due to diagnostic radiology, the genetically significant dose (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1972) and the per-capita effective dose equivalent (ICRP, 1977). Finally, risk estimates have been made using the nominal risk factors recommended in the ICRP Publication 26 (ICRP, 1977).

METHODS

The assessment of the radiation exposure due to diagnostic radiology in FVG involved three phases: statistical data collection, dosimetric measurements and estimation of organ and collective doses.

In the first phase, a regionwide survey was carried out during 2 weeks in 1983 to collect information on frequency and types of examinations, and on the sex and age of those exposed. Questionnaires were sent to all the facilities to record details on every examination, including patient sex, age, weight, height, number and size of radiographs, and use of fluoroscopy and gonadal shielding. The reply rate was about 100%, with the exception of the private dental offices, whose reply rate was about 11%.

Detailed data concerning 35 800 examinations were collected. The annual number of each type of examination was estimated by correcting the number per week obtained from the survey with a factor accounting for seasonal variations in the examination rate. The correction factor was estimated from a sample of radiology workloads reported in the 1983 annual returns to the regional health service.

The collected data were entered into a computer and checked on input. Checks were carried out for plausible patient age and sex for the examination, plausible patient size with regard to age and sex, and for consistent values of technical parameters for the examination.

The subsequent analysis allowed the estimation of the relative frequency of each examination, the age and sex distribution, the mean number of radiographs, film area and fluoroscopy screening time, and the percentage use of gonad shields.

The survey frequency data combined with the values in the literature for examination doses identified which examinations contributed most to the collective doses of the population. These were then the object of the measurements in the second phase. Fourteen examinations were selected, which contributed 95% of the genetically significant dose (GSD) and 86% of the per-capita effective dose equivalent (EDE).

The minimum size of the sample of measurements necessary to achieve a given level of confidence for the collective doses was determined *a priori* on the basis of frequencies of, and expected doses from, the 14 examinations (Fabretto, 1984).

Measurements were performed at all the X-ray facilities of the region's public health service, which account for more than 80% of the total radiological workload in FVG, and concerned 1620 randomly selected patients. Before measurements were started on a particular piece of equipment, the correspondence between the control setting and the effective potential difference of the tube was checked using a step-wedge penetrameter. The total filtration was then determined from measurement of the first half value layer (HVL) at 60 kVp.

For practical purposes, examinations were divided into two categories, "simple" and "complex", according to the technique used. For "simple" examinations (head, chest radiography and photofluorography, shoulder, abdomen, pelvis, hip/femur, cervical spine, thoracic spine, lumbosacral spine, full spine, intravenous urography), measurements were made with TLDs (LiF TLD-100, Harshaw, USA) attached to the patient's skin to determine the entrance skin dose per radiograph and the doses to the compact organs close to the surface of the body, *i.e.* thyroid, breast and testes (Fig. 1).

For "complex" examinations (barium meal and barium enema), which involve a considerable amount of fluoroscopy and variations in beam direction and field size, entrance skin dose cannot be conveniently measured with TLDs. The exposure–area product for the complete examination was recorded with a flat, transparent ionisation chamber (Diamentor, PTW, Germany), attached to the tube housing. The Diamentor reading was then used to assess the equivalent total entrance dose for a suitable field (abdominal region for a barium enema and the kidney region for a barium meal). Doses to the patient were also measured with TLDs, as for simple examinations. Two TLDs were attached to the patient's back at breast level for the estimation of lung dose. Four additional TLDs monitored the geometry of irradiation at ovary level (Fig. 2).

The dosimetry system had had preliminary tests: doses down to 0.1 mGy could be measured with a standard deviation (SD) of less than 8%, while at 1 mGy the SD was between 3% and 4% of the mean. The minimum detectable dose was about 0.02 mGy. Dosemeter response varied by less than 5% over the range of diagnostic X-ray qualities, so no correction was made for energy dependence.

Calibration of the chamber in terms of R cm^2 was carried out for all X-ray equipment: exposure was measured with a 35 ml ionisation chamber in conjunction with a Farmer electrometer (Nuclear Enterprises, Great Britain) calibrated against a secondary standard.

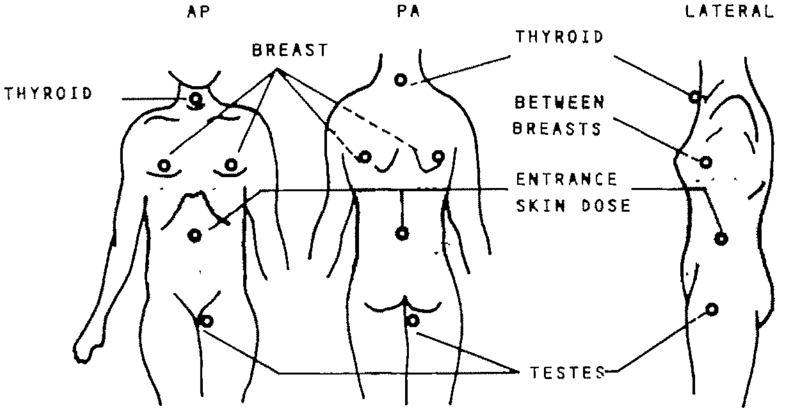

FIG 1.
Arrangement of TLDs on patients during "simple" examinations.

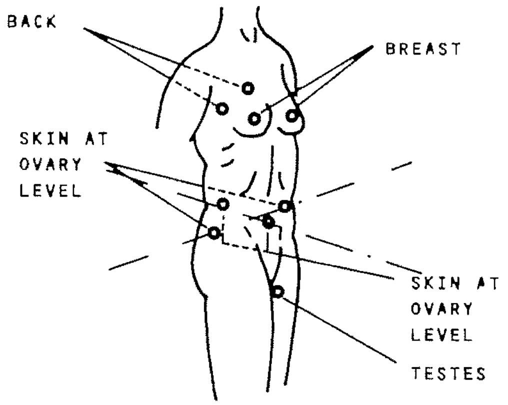

FIG 2.

Arrangement of TLDs on patients during "complex" examinations

An estimate of the beam area in the plane of the ionisation chamber was determined from the film exposure.

In the third phase, organ doses were derived from entrance doses for every examination of the sample. Thyroid and testes doses were estimated directly from TLD responses, while breast TLD measurements were converted to mean breast dose using factors to account for attenuation in the breast and the different composition of breast and muscle. Attenuation correction factors were 0.7 for the antero-posterior (AP) projections, 1.9 for the postero-anterior (PA) projections and 1.4 for the lateral (LAT) projections. Breast tissue composition was assumed to be a 50:50 mixture of water and fat, resulting in a further correction factor of 0.7. For complex examinations, lung dose was derived by taking the average response of the four TLDs at breast level.

Doses for other organs were derived from TLD measurements of entrance skin dose or from the exposure–area product for each examination of the sample, using the Monte Carlo conversion factors calculated at the NRPB (Jones & Wall, 1985). These factors relate the doses to 20 organs of an anthropomorphic phantom to the entrance skin dose for a set of 22 exposures covering the range of conditions found in the selected diagnostic procedures. The actual conversion factor for each exposure of the sample was derived by interpolating the NRPB conversion factors according to the corrected value of the voltage and the measured total filtration of the tube

For complex examinations, a weighted combination of AP and PA Monte Carlo conversion factors was used, with weightings given by front and back TLD readings, respectively.

Doses to an individual patient were calculated for the organs recommended in ICRP 26 (lung, ovaries, bone, red bone marrow) and for the "remainder", which includes the five organs or tissues receiving the highest doses during an examination. Examinations on children (under 15 years) could not be treated separately, but they represented only 8% of all examinations.

Estimates of organ doses for the other examination types were derived from the literature (Flatby et al, 1974; US Department of Health, Education and Welfare (DHEW), 1976; Wall et al, 1979, 1980; Hashizume et al, 1981; Beentjes & Glas, 1984; Drexler et al, 1984; Jankowski, 1984)

How representative the sample measurements are is shown by a comparison of the mean number of radiographs taken per examination in both the frequency survey and the measurement sample. Assuming that the mean dose is proportional to the mean number of radiographs per examination, a better estimate of the "true" mean doses can be obtained by correcting the sample mean doses with the ratio (number of films per examination of the statistical survey)/(corresponding value of the sample). The value of this ratio was close to unity for most examinations, the major exceptions being the abdominal and full spine examinations, found to have correction factors of about 1.4.

The estimation of the annual GSD to a population requires information on the age and sex distribution of the population, together with data on the child expectancy of the exposed individuals. Estimates of these data for the population of FVG were made from the regional health service's database. The population was divided into groups according to age and sex, and the mean mortality rate and the maternity/paternity rate were derived for every group (Padovani et al, 1985). The child expectancy for the population of FVG in 1983 was then calculated on the assumption that the mortality and fertility rates will not change significantly in the future. Moreover, the child expectancy of an exposed individual was taken to be equal to that of an average individual of the same age and sex. Results are given in Table I.

TABLE I

CHILD EXPECTANCY BY AGE AND SEX FOR THE POPULATION OF FVG IN 1983

Age band (years)	Male	Female
0	1.00	1.12
1–4	1.01	1.12
5–9	1.01	1.13
10–14	1.01	1.13
15–19	1.01	1.10
20–24	0.97	0.93
25–29	0.76	0.60
30–34	0.47	0.30
35–39	0.23	0.12
40–44	0.09	0.03
45–49	0.03	0.01
50–54	0.01	0.00
>55	0.00	0.00

TABLE II

NUMBER OF DIAGNOSTIC RADIOLOGICAL EXAMINATIONS IN FVG IN 1983

	No. (thousands) of non-dental X-ray examinations (SE)	No. (thousands) of dental X-ray examinations (SE)	No. (thousands) of all X-ray examinations (SE)
Male	477 (13)	63 (46)	540 (48)
Female	451 (13)	85 (46)	536 (48)
Totals	928 (18)	148 (65)	1076 (67)

SE = standard error.

RESULTS

Frequency survey

The total number of examinations is shown in Table II. The annual rate, inclusive of dental examinations, was 864 examinations per 1000 population. This rate is comparable with about 1000 examinations per 1000 population in developed countries (UNSCEAR, 1982). Males underwent a slightly greater number of examinations (887 per 1000) than females (807 per 1000).

The frequency distribution of examinations by age and sex is shown in Fig. 3 as the number of examinations per 1000 population in a given age–sex group. It indicates that the probability of undergoing an X-ray examination increases gradually with age. The lowest frequency is observed in children under 2 years, for whom it is one-third of the mean value for the entire population, while in the male group aged 60 years or more, it reaches the maximum, with a value 1.5 times higher than the average. People older than 50 years, who are 36% of the FVG population, underwent 45% of all the examinations.

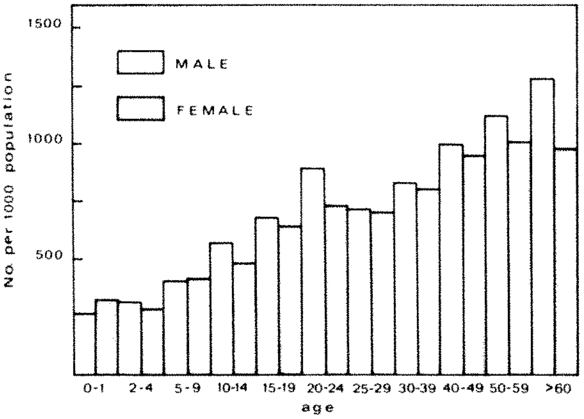

FIG. 3.

Frequency of X-ray examinations performed in FVG in 1983 as a function of age and sex. Each value represents the annual number of examinations per 1000 population in a given age–sex group.

The age distribution of the examined population varies markedly with the examination type: the number of head examinations hardly varies with age; heart and femur examinations are performed frequently for older individuals; full spine and extremity examinations have a peak frequency in teenagers, while abdomen, pelvis and urographic examinations are relatively frequently performed on neonates.

The relative frequencies of various types of examinations are reported in Table III. Chest examinations account for 37% of all examinations; dental and extremity examinations each account for 14% of the total. Computed tomography accounts for 1.5% of all

TABLE III

DISTRIBUTION BY TYPE OF DIAGNOSTIC RADIOLOGICAL EXAMINATIONS IN FVG IN 1983

Type of examination	Male (%)	Female (%)	Male and female (%)
Head	4.66	5.07	4.86
Dental radiography	11.63	15.86	13.74
Chest, heart	30.34	25.53	28.12
Chest photofluorography	10.57	8.07	9.33
Mammography	0.00	1.50	0.75
Abdomen	2.54	2.44	2.49
Barium meal	2.71	2.88	2.78
Barium enema	1.06	1.28	1.17
Cholecystography	0.77	1.42	1.10
Cholangiography	0.29	0.47	0.34
Intravenous urography	1.77	1.21	1.49
Pelvis	2.12	3.51	2.81
Full spine	0.96	1.58	1.27
Cervical spine	2.44	3.70	3.07
Thoracic spine	1.29	1.71	1.50
Lumbosacral spine	3.77	4.73	4.25
Shoulder, clavicle	2.27	2.14	2.20
Upper extremities	6.86	4.44	5.66
Hip, femur	1.60	2.13	1.87
Lower extremities	8.69	7.54	8.12
Head CT	0.92	0.88	0.90
Body CT	0.66	0.56	0.62
Angiography	0.43	0.21	0.31
Other	0.82	0.84	0.83
Totals	100	100	100

TABLE IV

MEANS AND MEDIANS OF THE NUMBER OF EXPOSURES AND RADIOGRAPHS PER EXAMINATION

Type of examination	No. of exposures		No. of radiographs	
	Mean	Median	Mean	Median
Head	3.9	3	3.5	3
Dental, orthopantomography	1.0	1	1.0	1
Dental, intraoral	2.2	1	2.2	1
Angiography, head	54.6	24		
Chest, radiography	1.7	1	1.7	1
Chest, photofluorography	1.0	1	1.0	1
Heart	2.3	2	2.3	2
Ribs	3.3	3	3.2	3
Mammography	5.3	6	5.0	5
Cardiac angiography	29.7	21		
Abdomen	2.1	2	2.0	2
Barium meal (swallow)	11.7	9	5.8	5
Barium meal (stomach, duodenum)	15.0	14	8.5	8
Barium meal (follow-through)	19.2	16	10.9	9
Barium enema	10.5	10	9.4	9
Cholecystography	4.4	4	2.9	3
Cholangiography	8.8	9	6.9	7
Intravenous urography	10.2	10	9.8	10
Cystography	9.1	9	7.0	6
Angiography, abdomen	24.0	13	12.6	
Pelvis	1.8	1	1.6	1
Full spine	5.8	6	5.2	5
Cervical spine	2.8	2	2.5	2
Thoracic spine	2.5	2	2.3	2
Lumbosacral spine	3.4	3	3.0	3
Myelography	13.2	10	10.1	8
Operative cholangiography	3.0	2	2.8	2
Shoulder, clavicle	2.2	2	2.1	2
Arm	2.2	2	1.9	2
Elbow	2.3	2	1.8	2
Forearm, wrist and hand	2.3	2	1.6	1
Hip, femur	2.3	2	2.2	2
Knee	3.0	2	2.6	2
Lower leg and foot	2.7	2	2.2	2
Angiography, peripheral	26.7	7		
Others	8.9	7	7.3	5
All	3.1	2	2.6	2

examinations (13 per 1000 population), with about 60% of the total concerning the head. The examinations are almost equally divided between males and females, the major exceptions being mammography and cholecystography. Examinations concerning the respiratory organs, the gastrointestinal tract (with the exception of barium enema) and the urogenital organs are more frequent in males, while spine, pelvis and hip examinations are more frequent in females.

The mean number of exposures and of radiographs for each type of examination are shown in Table IV. The total mean number of exposures per examination is 3.1, whereas the total mean number of radiographs is 2.6, consistent with other countries' results (Fig. 4). Angiography involves the greatest number of exposures (55 for angiography of the head). Of the most frequent examinations, a great number of exposures (10–20) are taken during barium meal, urographic and barium enema studies.

Estimates of the percentage of cases where tomograms are taken are also made for the various types of examinations. cholangiography and urography are the only examinations that significantly involve tomographic procedures (in 48% and 41% of cases, with a mean number of five and four exposures, respectively), while other examinations make use of tomography in less than 2% of cases.

About 8% of all examinations involve fluoroscopy.

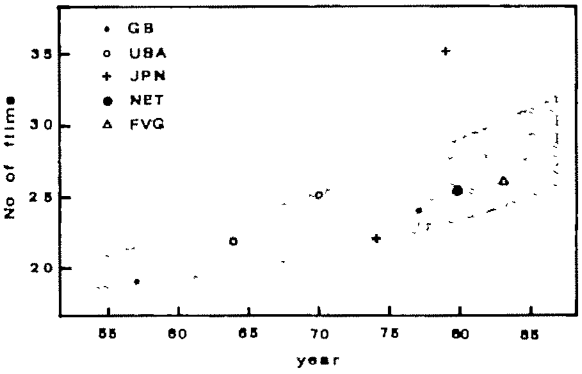

Fig. 4.

Mean number of radiographs per examination in FVG (△) in 1983 compared with the values assessed in other national studies Data are drawn from ○ DHEW, 1973 (USA); • Kendall et al, 1980 (Great Britain); + Hashizume, 1981 (Japan); ● Beentjes & Glas, 1984 (Netherlands).

Most angiographic studies and all cardiac catheterisation, barium meal and barium enema examinations involve fluoroscopy. In almost all of these examinations radiographs are also taken. The mean screening time is 3.5 min.

The use of gonad shields is reported in only 2.1% of examinations. There is a variation in the percentage use with the age of the patient: for children under 10 years, a 10% use is reported for males and 16% for females, while for people of reproductive age it falls to 2.1%. Gonad shields seem to be used properly in few cases: 10% of examinations where the use of a gonad shield is desirable compared with 9% in those where it is less important. The examinations on children most commonly associated with the use of gonad shields are urography, full spine, head, lower extremities and chest.

Dosimetric measurements

Table V shows the results of measurements of entrance skin dose during the commonest radiographic projections of the 12 simple examinations for a random sample of 1367 patients. Table VI shows the Diamentor measurements of total exposure–area product made during the two complex examinations. Mean values of the number of radiographs and applied potential for each examination are also given in the tables. The values of applied potential show a small coefficient of variation, from 8% for chest PA photofluorography to 23% for AP projections of lumbosacral spine examination. Entrance skin doses span very wide ranges, with the extremes covering an overall mean factor of 40 (from 6 for chest photofluorography to 270 for chest PA radiography). They are influenced by several factors, such as body size, examination method, equipment performance and personnel training. Distributions are often very skew, with a few strongly deviating observations which heavily influence the mean and the standard deviation values, so that the mean only approximately locates the dose distribution.

Mean doses in various body organs for the 14 selected examinations are given in Table VII for each type of examination. In the second column, the ratio of the average exposure numbers assessed in the statistical survey to those in the sample gives the magnitude of the corrections made on the sample doses.

For some organs (thyroid, breast, testes and lungs) Monte Carlo doses derived from skin entrance dose are compared with doses measured with TLDs. It can be seen that the remainder dose is often the highest dose to an organ during an examination. This happens every time there are some of the remaining organs in the useful beam, as in the examinations of abdomen, pelvis and lumbosacral spine, and intravenous urography (IVU) and barium meal and barium enema studies.

The overall highest mean dose per examination to an organ (excluding the remainder) is the dose to the thyroid measured during the examination of the thoracic spine (16.4 mGy), followed by that to the ovaries recorded during barium enema examination (15.3 mGy). The highest doses to the testes, breast, red marrow, lungs and bone are delivered, respectively, by examinations of the pelvis, IVU, and barium enema and barium meal examinations.

The spread of doses between individuals is very large, with coefficients of variation greater than 100%. Dose distributions vary with the examination type and exhibit a positive asymmetry, with the median between 40% and 75% of the mean. Highest positive asymmetries pertain to the distributions of measured doses to the organs situated at the border of the radiation field. For instance, in an abdominal examination, the mean doses to the breast and testes are heavily influenced by a few high doses delivered when the organs are in the useful radiation beam and the medians are, respectively, 23% and 19% of the mean, while entrance skin doses have a median 75% of the mean for females and 86% for males.

The comparison between the doses measured with TLDs and Monte Carlo doses is interesting, as it demonstrates the limitations of the Monte Carlo method in simulating actual irradiation. Coefficients were calculated for a set of radiographic parameters (focus-to-skin distance, projection, field size and position) selected to represent the typical conditions for a given examination, but these parameters vary considerably, so that the method often underestimates the complete range of doses received in practice, as the deviations from the normal distribution of the measured doses indicate.

Table VIII shows the contribution of each examination type to the collective organ dose per 1000 population. Generally, the resultant collective dose to an organ cannot be attributed to one dominating type of examination. For a given organ, we can identify two examinations which contribute together over 50% to the collective dose, namely pelvic examinations and

TABLE V

MEANS AND STANDARD DEVIATIONS OF ENTRANCE SKIN DOSES MEASURED DURING THE COMMONEST RADIOGRAPHIC PROJECTIONS OF THE "SIMPLE" EXAMINATIONS ON A RANDOM SAMPLE OF 1367 PATIENTS

Examination	No. of observed examinations	No. of radiographs per examination (SD)	Projection	No. of observations	Applied potential (SD) (kV)	Entrance skin dose per radiograph (SD) (mGy)
Head	93	3.08 (1.27)	AP	58	71.4 (8.2)	4.10 (2.90)
			PA	71	73.0 (6.7)	4.62 (2.86)
			LAT	111	64.6 (8.0)	2.62 (1.86)
			OBL	46	76.3 (7.1)	4.61 (3.40)
Chest radiography	454	1.54 (0.62)	AP	83	64.2 (9.0)	1.27 (1.68)
			PA	395	74.4 (16.3)	0.53 (0.74)
			LAT	207	87.8 (14.1)	2.66 (2.80)
Chest photofluorography	127	1.00 (0.00)	PA	127	73.2 (6.2)	2.64 (0.91)
Shoulder	61	2.36 (0.86)	AP	113	62.3 (7.6)	1.40 (1.59)
			OBL	25	62.4 (9.1)	2.55 (3.17)
Abdomen	93	1.45 (0.55)	AP	79	75.4 (9.0)	8.09 (4.70)
			PA	24	74.1 (12.9)	6.56 (3.14)
Pelvis	93	1.43 (0.80)	AP	118	67.4 (9.0)	10.6 (12.4)
Hip, femur	46	1.85 (0.76)	AP	66	68.7 (9.4)	3.69 (2.73)
			LAT	19	62.1 (6.0)	4.53 (3.73)
Cervical spine	87	3.07 (1.04)	AP	88	73.8 (10.7)	1.82 (1.89)
			LAT	92	72.2 (10.7)	1.58 (1.31)
			OBL	81	82.3 (17.3)	1.67 (1.18)
Thoracic spine	34	2.24 (1.39)	AP	44	75.0 (17.0)	10.8 (16.7)
			LAT	32	72.5 (8.2)	18.7 (16.8)
Lumbosacral spine	124	3.15 (0.88)	AP	210	77.6 (17.9)	9.53 (8.29)
			LAT	122	85.3 (16.4)	28.3 (24.9)
			LSJ	58	93.3 (17.2)	24.9 (18.9)
Intravenous urography	130	10.13 (3.48)	AP (kidney)	565	71.4 (8.1)	9.15 (6.19)
			AP (abdomen)	430	72.2 (7.4)	6.91 (4.55)
			AP (bladder)	161	76.4 (11.0)	7.16 (6.63)
			PA (kidney)	21	85.1 (10.7)	5.81 (1.68)
			PA (abdomen)	39	70.6 (6.6)	5.53 (2.59)

SD = standard deviation.

IVU for testes; barium enema and lumbosacral spine examinations for ovaries; IVU and chest radiography for breast; barium meal and barium enema for red marrow and total bone; barium meal and chest radiography for lungs; thoracic and cervical spine examinations for thyroid; and barium meal and lumbosacral spine examinations for the remainder.

Mean annual individual doses to the various organs

TABLE VI

MEANS OF THE DIAMENTOR MEASUREMENTS OF TOTAL EXPOSURE–AREA PRODUCT MADE DURING THE "COMPLEX" EXAMINATIONS ON A RANDOM SAMPLE OF 253 PATIENTS

Examination	No of observed examinations	No of radiographs per examination (SD)	Screening time (SD) (s)	Applied potential (SD) (kV)	Exposure–area product (SD) (R cm^2)
Barium meal	153	13.9 (7.6)	337 (410)	88.8 (18.1)	4377 (3055)
Barium enema	100	9.8 (3.8)	239 (206)	100.1 (18.6)	4765 (3485)

SD = standard deviation.

TABLE VII

Mean organ doses (mGy) by examination type

Examination	Correction factor	Mean dose received (% coefficient of variation) (mGy)											
		Testes		Ovaries	Breast		Bone marrow	Lung		Thyroid		Bone	Remainder
		TLD	MC	MC	TLD	MC	MC	TLD	MC	TLD	MC	MC	MC
Head	1.27		*	*		*	0 17 (89)		0.01 (117)	1.61 (177)	0.30 (116)	0.99 (85)	0.42 (73)
Chest radiography	1 10		*	*	0.29 (112)	0 45 (224)	0.12 (164)		0.45 (156)	0.34 (265)	0.11 (290)	0 25 (161)	0.17 (79)
Chest photofluorography	1.00		*	*	0 14 (7)	0.15 (66)	0.26 (41)		0 91 (39)	0.07 (26)	0 08 (48)	0.59 (38)	0.23 (22)
Shoulder	0 93		*	*	0.40 (168)	0.01 (125)	0.02 (123)		0.06 (123)	1 18 (195)	0.02 (125)	0.07 (127)	0.01 (118)
Abdomen	1.45	2.33 (177)	0.43 (97)	2.33 (87)	0.90 (213)	0 03 (95)	0.64 (83)		0.09 (88)		*	0 82 (76)	3.63 (43)
Pelvis	1.26	8 09 (104)	10.54 (102)	2.38 (100)	0 04 (106)	*	0.34 (103)		*		*	0.63 (101)	3.75 (47)
Hip, femur	1.24	5 68 (113)	1 80 (106)	0 51 (114)	0.02 (77)	*	0.07 (116)		*		*	0.22 (114)	0 59 (58)
Full spine	1.38	2.82 (191)	0.04 (100)	2.27 (88)	3 13 (117)	0 52 (163)	1 24 (74)		2.32 (112)	7.76 (87)	2.73 (142)	2 34 (54)	3.53 (38)
Cervical spine	0.91		*	*		*	0 03 (122)		0 02 (118)	4 00 (98)	1.16 (151)	0.15 (119)	0.02 (94)
Thoracic spine	1 12		*	*	0.68 (133)	0.59 (168)	0.73 (114)		2 63 (106)	16.45 (288)	2.38 (183)	1 79 (115)	0 97 (69)
Lumbosacral spine	1 08	1.71 (262)	0.06 (98)	3.85 (83)	0 47 (300)	0.08 (93)	1.07 (79)		0.34 (92)		*	1.36 (79)	5.03 (39)
Intravenous urography	1 01	7.57 (134)	2.27 (131)	5 05 (90)	8.79 (16)	0.22 (99)	1 44 (77)		0.66 (101)		*	2.34 (77)	12.64 (41)
Barium meal	1 27	0 15 (120)	*	1.51 (96)	1 85 (177)	0.63 (104)	4.81 (57)	9 79 (123)	2.71 (77)	0 73 (114)	*	7.36 (57)	22.61 (52)
Barium enema	1.07	2.26 (152)	2.33 (112)	15 34 (91)	0 50 (267)	0.19 (111)	6.65 (57)	2 39 (173)	0.69 (85)	0.11 (85)	*	7.18 (59)	17 53 (53)

*Represents doses lower than 0.01 mGy. TLD doses to testes and breast have been measured only for males and females, respectively, whereas Monte Carlo (MC) doses have been calculated for every patient, irrespective of sex.

from all the selected types of examinations are given in Table IX. By using the risk factors suggested by the ICRP for these organs, the approximate number of fatal cancers in these organs induced by 1 year's practice of these 14 examinations in the FVG region can be estimated. These risk estimates are very crude, as the risk factors are an average for both sexes and for all ages and probably lead to overestimation of the likely number of effects. With the population standing at 1 246 000, the expected fatal malignancies are estimated to be one cancer in lung, one in breast, and about one case of leukaemia. The high value of the remainder dose would predict 8.6 cases of cancer, but for the purpose of risk estimation, more realistic and specific factors for these organs are required, rather than the same ICRP factor of 10^{-3} Sv^{-1} for every organ.

The effective dose equivalent and the annual per-capita effective dose equivalent per examination are given in Table X for all types of examination. The annual per-capita effective dose equivalent in 1983 from diagnostic radiology in FVG is 0.848 mSv, of the same order as the annual contribution from natural radiation sources.

These doses may provide an approximate prediction of the likelihood of malignancy induction and genetic detriment by using the nominal total risk factor of 1.65×10^{-2} Sv^{-1} suggested by the ICRP. The collective effective dose equivalent to the FVG population for diagnostic radiology in 1983 is about 1056 man.Sv.

TABLE VIII

COLLECTIVE ORGAN DOSES PER 1000 POPULATION BY EXAMINATION TYPE FROM THE 14 EXAMINATIONS SELECTED FOR THE DOSIMETRIC MEASUREMENTS

Examination	No. of examinations per 1000	Collective organ dose (man.mGy per 1000 population)							
		Testes	Ovaries	Breast	Bone marrow	Lung	Thyroid	Bone	Remainder
Head	42	< 0.4	< 0.4	< 0.4	7.0	0.3	67.6	41.5	17.6
Chest radiography	222	< 2.2	< 2.2	64.2	26.6	100.5	75.0	56.4	37.7
Chest photofluorography	80	< 0.8	< 0.8	11.2	20.8	72.8	5.6	47.2	18.6
Shoulder	19	< 0.2	< 0.2	7.6	0.3	1.2	22.4	1.4	0.1
Abdomen	22	50.1	50.0	19.3	13.7	1.9	< 0.2	17.6	78.0
Pelvis	24	196.6	57.9	1.0	8.2	< 0.2	< 0.2	15.2	91.1
Hip, femur	16	91.0	8.2	0.3	1.2	< 0.2	< 0.2	3.5	9.4
Full spine	11	31.1	25.0	34.4	13.6	25.5	85.4	25.7	38.8
Cervical spine	27	< 0.3	< 0.3	< 0.3	0.9	0.5	106.1	4.0	0.6
Thoracic spine	13	< 0.1	< 0.1	8.8	9.4	33.9	212.1	23.1	12.5
Lumbosacral spine	37	62.9	141.4	17.4	39.4	12.4	< 0.4	49.8	184.5
Intravenous urography	13	97.6	64.9	113.4	18.3	8.4	< 0.1	29.7	163.1
Barium meal	24	3.5	36.4	44.4	115.4	235.0	17.5	176.6	542.9
Barium enema	10	22.8	154.9	5.1	67.2	24.1	1.1	72.5	177.1
Total	559	556	539	327	342	517	593	564	1372

The collective organ doses for the whole population in FVG are 1246 times the doses per 1000 population. Collective doses to gonads and breast do not take into account the sex distribution of the patients undergoing a given examination. The totals do not include the upper dose limits (marked <), which would contribute less than 1% to the collective doses

Within the limits already expressed, the associated risk is estimated to be about 17 cases of serious late injury. Excluding the genetic detriment, the number of X-ray-induced malignancies is about 14, which is to be compared with an estimated annual incidence of malignant diseases of 4000 cases (3777 deaths from cancer have been registered in FVG in 1978 (Istituto Centrale di Statistica (ISTAT), 1978), corresponding to a rate of 303 deaths per 100 000 population).

TABLE IX

MEAN ANNUAL ORGAN DOSE PER INDIVIDUAL AND CASES OF FATAL INJURY FROM EXPOSURE TO THE 14 SELECTED X-RAY EXAMINATIONS IN FVG IN 1983

Organ	Dose (mGy)	ICRP risk (10^{-4} Sv^{-1})	No of cases in FVG
Testes	0.56	40	2.7
Ovaries	0.54		
Breast	0.33	25	1.0
Red bone marrow	0.34	20	0.9
Lungs	0.52	20	1.1
Thyroid	0.59	5	0.4
Total bone	0.56	5	0.4
Remainder	1.37	50	8.6

Collective risk estimates indicate that the greatest risk is due to the barium meal examination, with an associated risk of 4.6 cases from 1 year's diagnostic practice Equal risks (1.9 cases) are carried by lumbosacral spine examinations, IVUs and barium enemas, followed by the examination of the lungs (radiography and photofluorography) and of the pelvis, with 1.2 cases each.

In Table X, the risk estimates per examination performed, calculated by using the ICRP total risk factor, are also given. Barium meal, barium enema and IVU examinations carry the highest risks, with more than 100 cases per million examinations, while examinations of the head, chest, shoulder and cervical spine carry a risk of 2–4 cases per million. Other examinations are associated with a risk of 10–50 cases per million, comparable with the risk of 50 per million associated with the recommended annual dose limit for members of the public in ICRP Publication 26.

Genetically significant doses have been determined separately for males and females, so they are not directly additive (Table X). Examinations of the pelvis, hip and femur, and IVU, in that order, contribute more than 50% to the GSD for males, while for females an analogous contribution is given by lumbosacral spine, barium enema and full spine examinations The annual GSD to the population is 0.253 mSv compared with a mean gonadal dose of 0.547 mSv. This

TABLE X

GENETICALLY SIGNIFICANT DOSE (GSD), EFFECTIVE DOSE EQUIVALENT (H_E), ANNUAL PER-CAPITA EFFECTIVE DOSE EQUIVALENT (EDE), INDIVIDUAL RISK AND COLLECTIVE RISK PER EXAMINATION BY TYPE OF EXAMINATION

Examination	GSD (μSv)		H_E (μSv)	EDE (μSv)	Risk per examination ($\times 10^{-6}$)	No. of cases in FVG
	Males	Females				
Head	< 0.2	< 0.2	224	9	4	0.2
Chest radiography	< 0.9	< 0.9	181	40	3	0.8
Chest photofluorography	< 0.3	< 0.3	250	20	4	0.4
Shoulder	< 0.1	< 0.1	109	2	2	0.0
Abdomen	26	20	1919	41	32	0.8
Pelvis	77	25	2325	56	38	1.2
Hip, femur	50	2	879	14	15	0.3
Full spine	27	28	2878	32	47	0.7
Cervical spine	< 0.1	< 0.1	137	4	2	0.1
Thoracic spine	< 0.1	< 0.1	1343	17	22	0.4
Lumbosacral spine	31	65	2509	92	41	1.9
Intravenous urography	46	28	7074	91	117	1.9
Barium meal	2	14	9266	222	153	4.6
Barium enema	5	30	8968	91	148	1.9
Others	10	18		115		2.4
Total	253			848		17.4
Standard error	17			18		

The ICRP total risk factor of 165×10^{-4} Sv^{-1} has been used. The total GSD does not include the upper dose limits (marked <), which would contribute less than 1%.

value is of the same order as those recently estimated in industrialised countries, ranging from 0.120 mSv for Great Britain (Darby et al, 1980) to 0.420 mSv for Sweden (Bengtsson et al, 1978).

By using the risk factor of genetic injury suggested by the ICRP (10^{-2} Sv^{-1}) for the first two generations and an additional equal risk for all the succeeding generations, the resultant risk at equilibrium is estimated to be 2.5 cases per year. For comparison, it is estimated that, of babies born in FVG per year, about 200 suffer from congenital malformations (Mastroiacovo et al, 1982).

CONCLUSION

This survey has assessed the impact of radiological practice in FVG, through the determination of frequencies, doses and risks of examinations.

The frequency results indicate that medical radiology in FVG compares with that of other developed countries. The distribution of procedures shows that the role of complex examinations, *e.g.* CT procedures, becomes more and more important, photofluorography in mass chest procedures is increasingly replaced by radiography, and mammography appears to be still a clinical rather than a screening examination.

The spread of individual patient doses is quite large, usually two orders of magnitude or more, suggesting that a relevant dose reduction can be readily achieved with available techniques. Moreover, the main efforts for collective dose reduction should mainly concern a few types of examinations. Further indications for dose reduction may arise from a close comparison with analogous surveys in other countries.

Risk estimates, even with the associated large uncertainties, indicate that, at the moment, neither individual nor collective risks constitute any contra-indication to clinically indicated examinations. Nevertheless, it is felt that radiation protection of the patient is still far from optimal and the introduction of a code of practice for dose limitation in medical exposure (by far the largest component of collective dose from man-made radiation sources) should be considered.

ACKNOWLEDGMENTS

We would like to thank both patients and staff of all the X-ray departments visited for their co-operation. We are especially grateful to our technicians who diligently performed the measurements and data entry. This work was partially supported by CEC Contract No. BIO-516-I(S).

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Book reviews

Advances in Cancer Control Health care financing and research. Ed. by L. E. Mortenson, Paul F. Engstrom and Paul N. Anderson, xvii+480, 1986 (Alan R. Liss, Inc., New York), £53.00.
ISBN 0–8451–5066–9

This American book is about the changes in attitudes towards the control of cancer and covers aspects of health care financing and research. It is a multi-author publication of eight sections, each of which is introduced by an authority on a particular area of cancer control

It opens with reference to the National Cancer Institute's objectives for the year 2000, indicating the potential reduction in mortality which might be achieved by the application of existing knowledge in areas of prevention, screening and treatment. The total reduction in mortality, it is suggested, could be as high as 40–50%.

There is an interesting account of the result of a community hospital oncology programme in which a number of hospitals received financial help to develop systems to identify important new advances and ensure rapid implementation. Although the initial outcome might, at first, be considered disappointing, the systems developed suggest much thought for the future There is an interesting section on financial aspects of health care, covering widely differing subjects ranging from the comparative costs of home and hospital treatment, to cost-effectiveness of liver scanning in newly diagnosed colo-rectal carcinoma and the impact of health care economics on the selection of new radiation therapy equipment. Although much of this applies to the American methods of financing, there is a great deal of interest and relevance to the British scene, in our present atmosphere of cost-effectiveness in the NHS.

In a section on clinical practice trends, thoughts are expressed not only about the battle of funding the costs of scientific developments, but on problems such as the safe disposal of the varied waste products from oncological units, such as disposable plastic objects, glass and metals.

There are also a number of clinically orientated papers such as that giving an account of intraoperative irradiation when patients are transferred during surgical procedures to the linear accelerator treatment room. An account is given of changes in post-menopausal hormone prescribing habits, to assess the value of continuing medical education programmes, and there are papers on cancer pain management as well as oncology nursing trends

This is an interesting, thought-provoking book, arriving at a time when we are having to keep costs in mind. It will be of particular value to those in oncology units and to community physicians and of considerable interest to many hospital general managers.

BRENDAN HALE

Radiation Risks to the Developing Nervous System. By H. Kriegel, W. Schmahl, G. B Gerber and F. E. Stieve, pp. xii+435, 1986 (Gustav Fischer, Stuttgart), DM110.
ISBN 3–437–11056–X (Stuttgart)
0–89574–225–X (New York)

This book represents the proceedings of an international symposium (produced in camera-ready format) jointly organised by the Commission of the European Communities (CEC, Brussels) and the Gesellschaft für Strahlenund Unweltorschung m.b.H (GSF, München), which was held at Neuherberg in June 1985 The topic, radiation risk to the developing nervous system, forms part of the Radiation Protection Programme of the CEC.

In an excellent introductory paper, Dr Mole first provides an historical update of the evidence for radiation damage to the developing nervous system in man. He concludes by asking a number of still unanswered questions. With respect to mechanisms, it is important to know whether the cells lost through death at mitosis can be replaced by additional unscheduled cell division This may be possible, as in other tissues after irradiation. However, it is uncertain whether the incorrect number of cells being in the wrong place at the wrong time leads to gross abnormalities in the nervous system. This is a controversial point, as is borne out by the published discussion on this paper (always a valuable part of a conference proceedings) and subsequent contributions

Clearly an answer to this and other points can be gained by a better understanding of the development of the nervous system. This was the topic of four contributions where both morphological and biochemical aspects of the differentiation of the central nervous system were discussed

By far the major bulk of the proceedings is made up of papers, a total of 21, on experimental studies of the effects of radiation on the developing nervous system. The effects of radiation alone or in combination with chemical toxins are considered. Only two contributions relate directly to the effects of intrauterine exposure in man; one being a reassessment of the neurological deficit of the survivors of the atomic bombing at Hiroshima and Nagasaki, now some 40 years after the event.

Amongst other points raised in the concluding round table discussion, a general consensus was reached that animal experiments can best be used to extrapolate mechanisms but not to obtain quantitative data for man.

This book, which is well presented, is of general interest to all those in the field of radiobiology, but clearly has a specific application to the area of radiological protection.

J. W HOPEWELL

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An investigation into the levels of radiation exposure in diagnostic examinations involving fluoroscopy

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ABSTRACT

In order to investigate the levels of radiation exposure resulting from fluoroscopic examinations, area–exposure product measurements were performed on 6532 patients whilst undergoing a variety of examinations at a large district general hospital. Results for both the same and different types of examinations, performed in two different X-ray rooms by a number of different radiologists, are compared in order to highlight some of the factors which influence the wide variations in patient exposure which frequently occur in radiological examinations. Variations in exposure of patients of different weights are also presented.

Approximately 12% of the total radiation dose to the UK population is due to man-made irradiation (NRPB, 1985). Of this, about 94% is due to medical procedures. Current and future legislation requires this irradiation to be kept as low as reasonably achievable (ALARA principle), taking social and economic factors into consideration.

Kendall et al (1980) suggest that about 21 million radiodiagnostic examinations are carried out annually in National Health Service hospitals in the UK. Fluoroscopic examinations, although comprising only about 6% of all radiological procedures (approximately 1.2 million examinations per year), are often high-dose investigations and, as such, represent an appreciable fraction of the total somatic population dose. Also, since a large proportion of all fluoroscopy concerns the abdominal region, and the frequency of use of gonad shields is still low (Wall et al, 1980), these types of examination contribute a large fraction of the genetically significant dose Indeed, all examinations which are likely to give high doses are worthy of special attention, it may be more important to consider the risk to the individual patient concerned, rather than the population as a whole (Moores et al, 1982). Various reports have been published indicating the ranges of doses delivered for particular examinations (Wall et al, 1980; Harrison et al, 1983; Kearton, 1983; Faulkner & Bramhall, 1985), but none of these has yet covered a range of fluoroscopic examinations.

Maximum permissible exposures have been defined for radiation workers and members of the general public, but no numerical guidance has been formulated as regards limits of exposures for patients undergoing standard radiological examinations. The results of this survey lend no support to the practicality of such a concept, albeit a measure of greater uniformity might well be achieved for simple radiographic procedures by the wider introduction of automatic exposure control (AEC) systems. Reject analyses have shown a fall in film reject rate after the introduction of a correctly installed AEC (Lewis, 1984, unpublished), and this in itself represents a reduction in the exposure per patient.

For the more elaborate investigations of clinical problems requiring fluoroscopic control, the situation is more complex because of the multiplicity of factors influencing the doses delivered These include not only the whole range of equipment from X-ray generator through intensifier to TV display but also the ability of patients to co-operate, and other variations in the clinical situation. While a properly implemented quality assurance programme should maintain equipment performance within appropriate limits, differences in patients and, perhaps, radiologists will always give rise to large and unpredictable variations in doses

There is no doubt that at present patients may receive vastly different radiation doses for the same examination under different circumstances, and some reports have considered possible causes for this. For example, Henshaw and Kennedy (1975) have reported wide variations in exposure rates to different intensifiers under automatic control, and Harrison et al (1983) suggest that the differences in technique adopted by different radiologists may be of significance in explaining doses which vary by as much as three orders of magnitude (Wall et al, 1980).

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Because of the importance of examinations involving fluoroscopy in relation to total population dose, both somatic and genetically significant, the present study was set up to assess the extent and range of patient exposure and the influence, if any, of some factors upon it. This was a large-scale survey conducted over a period of several years covering a wide range of such examinations and involved a number of different radiologists. Because data were recorded from a very large number of examinations, variations in such factors as size of patients and their ability to co-operate were evenly distributed amongst the radiologists and may be disregarded for comparison purposes.

METHOD

The survey was carried out in the main X-ray department at Blackpool Victoria Hospital, a large district general hospital serving a population of about 300 000, with a relatively high proportion of elderly people. During the period of data collection, fluoroscopic examinations were carried out by seven radiologists, working in a busy department with a high throughput of patients, suitable for a comprehensive study of this kind.

The two main fluoroscopy rooms at the time, referred to here as Rooms 1 and 2, were equipped with CGR and GEC X-ray installations, respectively. The CGR equipment in Room 1 was designed for remote control use, with an undercouch intensifier. Fluoroscopic exposures could be controlled either manually or automatically, but manual control was rarely used. Radiographic exposures could be recorded using either medium-speed calcium tungstate film-screen cassettes or a 105 mm camera. AEC was used for both these methods.

In Room 2, the GEC equipment was of the "traditional" undercouch tube/overcouch intensifier design. Both manual and automatic control were available for fluoroscopy. All films were produced by use of medium-speed film-screen cassettes, and radiography was manually controlled. It was anticipated that the study would provide useful comparative figures for patient exposures in the two rooms

The numbers and types of examinations carried out in these rooms were typical of those found in a busy district general hospital. They were distributed evenly between the two rooms, with the exception of barium enema examinations, which were rather more common in Room 2. Although each of the radiologists concerned worked predominantly in one room or the other, from personal preference, they all carried out a representative proportion of each type of examination.

Since the main aim of the study was to investigate the variations in radiation exposure to patients, and only to a lesser extent the magnitude of the exposures, it was felt that the most convenient method of measurement would be to use area–exposure product (Rcm^2) meters. Both rooms were fitted with Diamentor Rcm^2 meters. These are flat-plate ionisation chambers which are attached to the light beam/diaphragm housing. They are optically transparent so that where a light beam is used in positioning this is not adversely affected (Pychlau, 1984). The use of such equipment is recommended by the International Commission on Radiological Protection (ICRP, 1982), particularly for training purposes.

An advantage of using this type of meter in the survey was that it gives a measure of total energy imparted to the patient (Shrimpton et al, 1984), and, neglecting attenuation in the air, this is the same at all distances from the tube. Thus variations in focus–skin distances are accounted for. Also, the size of X-ray field, a very important but often neglected factor, is taken into account automatically, including any variations taking place during the fluoroscopic procedures.

The Diamentor meters used were capable of recording fluoroscopic and radiographic exposures independently. They were calibrated and checked periodically by the Regional Medical Physics Department. Subsequent references in this paper to exposure refer to the area–exposure product in units of Rcm^2.

For a period of approximately 3½ years, readings were taken from these meters for most fluoroscopic examinations in either room. For each examination, the following data were recorded:

sex, age, weight, date and type of examination, X-ray room number, radiologist, fluoroscopic exposure (Rcm^2), radiographic exposure (Rcm^2), screening time, films taken on 105 mm camera or cassette (choice available in Room 1 only), and automatic or manual control of fluoroscopy.

All these data were recorded on data sheets by the radiographers at the time of examination. The data were not analysed until the end of the period of collection. They were then numerically coded onto a second set of data sheets and entered manually into a digital minicomputer.

RESULTS

At the end of the survey period, data from 6531 examinations had been recorded The mean age of patients was 56 years and their mean weight was 65 kg. Of these examinations, 3405 were carried out on females, with mean age 57 years and mean weight 58 kg, and 3126 on males, mean age 55 years and mean weight 68 kg. The distributions of these parameters are shown in Figs 1 and 2 It can be seen that both are approximately normal distributions, with the age histogram negatively skewed.

Table I presents the number of patients examined by each radiologist in the two rooms. The personal preference of each radiologist for a particular room is apparent.

Although a total of 28 separate procedures were identified, the seven most common of these accounted

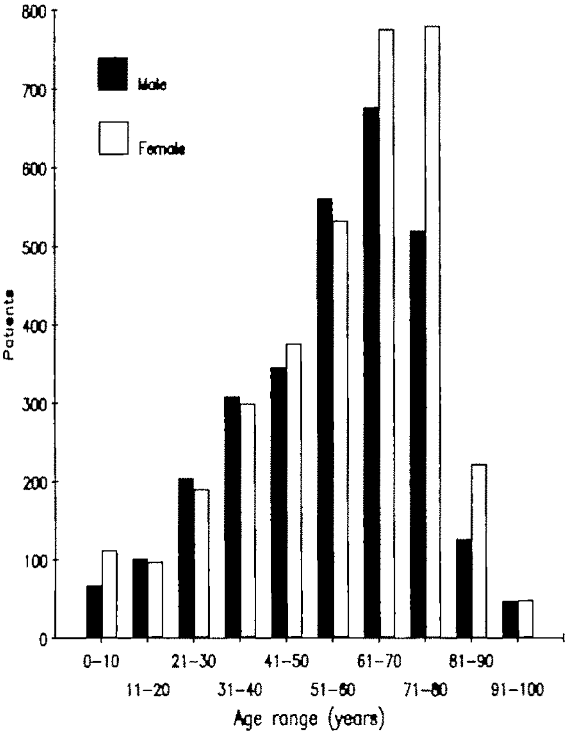

Fig. 1

Frequency distribution of patients' ages for both males and females undergoing screening procedures

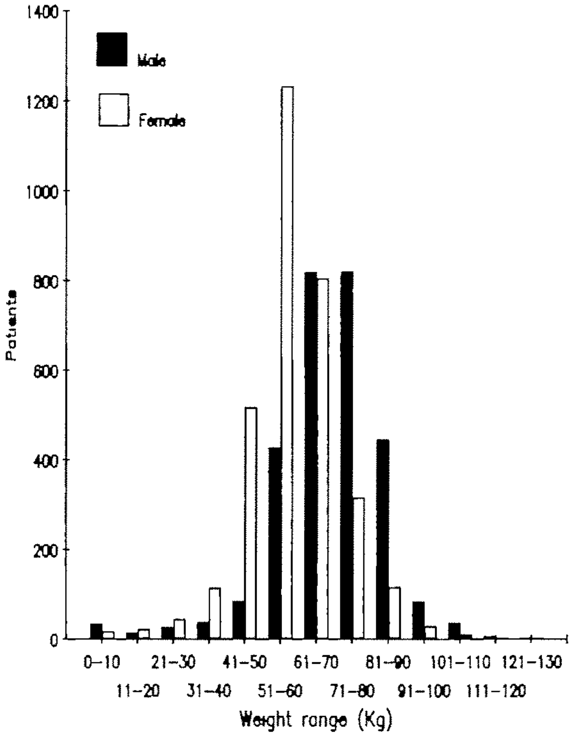

Fig 2

Frequency distribution of patients' weights for both males and females undergoing screening procedures.

for more than 95% of all examinations in this survey. Accordingly, Table II presents the number of patients undergoing each of these seven examinations in the two rooms, and all other examinations are grouped together. The examinations were distributed fairly evenly between the two rooms except for barium enemas: the difference here accounts almost exactly for the difference in total examination numbers. Although not shown in the table, it may be noted that the various types of examination were also evenly distributed among the seven radiologists.

TABLE I

Number of patients examined by each radiologist in each room

Radiologist	Room 1	Room 2	Both rooms
1	—	177	177
2	—	364	364
3	1088	13	1101
4	485	1137	1622
5	1025	336	1361
6	—	1504	1504
7	325	77	402
Total	2923	3608	6531

Because the distributions of the dose data were found to be extremely skewed it was decided that the median, 2½ and 97½ percentile values were the most suitable values to quote. However, for completeness, mean values have in most cases also been quoted. Table III presents the median, 2½ and 97½ percentile values of fluoroscopic and radiographic exposures for each radiologist and each room. It is immediately apparent that exposures are consistently lower in Room 1 and

TABLE II

Number of patients per examination in each room

Examination	Room 1	Room 2	Both rooms
Barium swallow	256	216	472
Barium meal	1538	1530	3068
Barium enema	585	1313	1898
Barium swallow + meal	155	170	325
Barium meal + follow-through	62	104	166
T-tube cholangiogram	107	48	155
Micturating cystogram	76	50	126
Others	144	177	321
Total	2923	3608	6531

TABLE III

MEDIAN FLUOROSCOPIC AND RADIOGRAPHIC EXPOSURES (RCM^2) DELIVERED BY EACH RADIOLOGIST IN EACH ROOM

Radiologist	Room 1						Room 2					
	Fluoroscopic			Radiographic			Fluoroscopic			Radiographic		
	Median	2½ percentiles	97½	Median	2½ percentiles	97½	Median	2½ percentiles	97½	Median	2½ percentiles	97½
1	—	—	—	—	—	—	1130 (1420)	150	4900	1760 (1950)	270	4640
2	—	—	—	—	—	—	880 (1110)	190	3520	1240 (1270)	140	2490
3	510 (610)	80	1720	240 (440)	30	2230	1040 (1206)	290	2890	690 (850)	240	1940
4	390 (560)	20	1990	190 (460)	10	2400	680 (840)	70	2700	720 (760)	10	1730
5	430 (510)	80	1440	330 (600)	40	2550	1040 (1380)	90	5150	1440 (1600)	70	3690
6	—	—	—	—	—	—	1020 (1180)	140	3240	1040 (1180)	120	2810
7	340 (430)	40	1400	400 (819)	40	3420	700 (830)	160	2890	940 (1250)	90	3740
All	440 (540)	220	1630	280 (540)	270	2580	890 (1090)	100	3390	980 (1120)	70	2980

Values in parentheses are means.

that there are also differences in the exposures delivered by each radiologist.

Table IV shows the medians of fluoroscopic and radiographic exposures and screening time for each of the seven most common examinations. These values are further subdivided in order to observe variation between examinations of males and females. As might be expected, the exposures are higher for male patients in almost every case although the screening times show little difference.

For convenience of display, the patients' weights were divided into 10 kg cells and in Fig. 3, the median fluoroscopic exposure rates (measured exposure divided by recorded screening time) are shown for male patients together with the 2½, and 97½ percentile values. There is seen to be a general increase in dose rate with

TABLE IV

MEDIAN FLUOROSCOPIC AND RADIOGRAPHIC EXPOSURES (RCM^2) AND SCREENING TIME FOR THE SEVEN MOST COMMON EXAMINATIONS

Examination	Fluoroscopic		Radiographic		Screening time (min)	
	Male	Female	Male	Female	Male	Female
Barium swallow	550 (670)	380 (500)	400 (600)	330 (510)	3.0 (3.4)	3.0 (3.2)
Barium meal	720 (880)	530 (690)	690 (840)	520 (670)	3.0 (3.7)	3.0 (3.8)
Barium enema	960 (1270)	850 (1050)	1190 (1390)	1120 (1250)	2.5 (3.0)	2.5 (2.9)
Barium swallow + meal	720 (890)	450 (660)	650 (830)	620 (740)	3.0 (3.5)	3.0 (3.6)
Barium meal + follow-through	530 (740)	410 (600)	430 (580)	590 (610)	2.5 (2.7)	2.0 (2.2)
T-tube cholangiogram	330 (410)	260 (350)	330 (380)	270 (370)	1.5 (2.1)	2.0 (2.2)
Micturating cystogram	160 (450)	110 (200)	80 (190)	80 (170)	2.5 (2.8)	2.0 (2.3)

Values in parentheses are means.

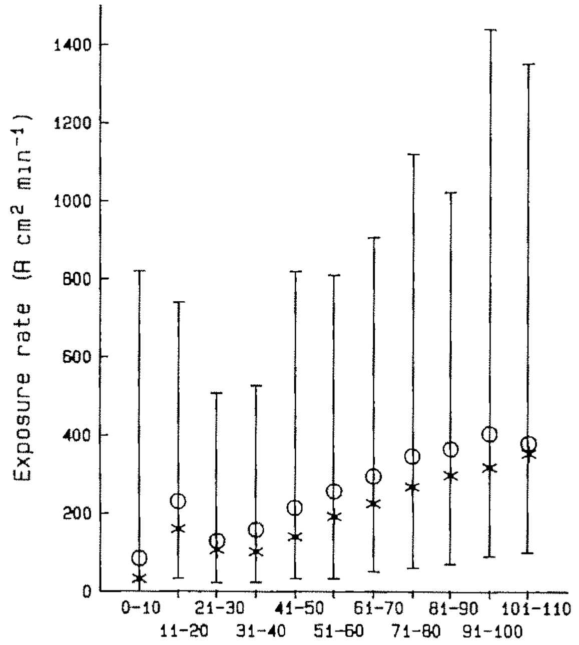

FIG 3.

Median, 2½ and 97½ percentiles of the exposure rate (Rcm² min⁻¹) for each weight range of male patients (mean values shown as ○)

increasing weight, as would be expected, but the spread of individual measurements as indicated by the 2½–97½ percentile range is large in each case. (A similar trend was noted for female patients.)

A Mann-Whitney *U*-test, the non-parametric equivalent of the unpaired *t*-test, was applied to the dose rate vs weight data for both males and females in order to assess the significance for the differences between the exposure rates of adjacent weight groups. Generally the results showed a significant difference between exposure rates of groups in the range 20–90 kg, while median values for groups outside this range were not significantly different. However, sometimes a significant level of difference between adjacent weight categories was noted for females but not for males and vice versa.

TABLE V

MEDIAN, 2½ AND 97½ PERCENTILES OF RADIOGRAPHIC EXPOSURES (RCM²) FOR BARIUM MEAL EXAMINATIONS USING FILM-SCREEN CASSETTE AND 105 MM CAMERA IN ROOM 1

	No of examinations	Median exposure (radiographic)	2½ percentiles	97½
Film-screen cassette	375	930 (1140)	70	3840
105 mm camera	949	210 (260)	50	840

Values in parentheses are means

The equipment in Room 1 offered the alternative of radiographic recording either using a film-screen cassette or on film in a 105 mm camera. In order to compare exposures by these two methods the values for the most common examination, barium meals, were examined. These results are presented in Table V.

Most fluoroscopy in Room 1 was under automatic mA control; however, in Room 2 the alternatives of manual and automatic control were investigated. Again using the example of barium meal examinations, the exposures are compared in Table VI. Only those examinations in which the use of automatic or manual selection was actually recorded are included in Tables V and VI.

DISCUSSION

Table III demonstrates that exposures to patients in Room 2 are much higher than in Room 1. The ratio of fluoroscopic exposures in these two rooms is 2.0, and the corresponding value for radiographic exposures is 3.5. By reference to Tables I and II, it is apparent that these differences are not due to the distribution of examinations or radiologists. The relevant factor is that of the equipment. Since the Diamentor readings are independent of the differences in geometry between the two installations (although if an exact comparison of skin doses were required, a correction would be necessary to account for the fact that the table top is between detector and patient in one room (Shrimpton & Wall, 1982)), it is concluded that the different fluoroscopic exposures are due primarily to the different input dose rates at which the intensifiers are operating. Faulkner and Bramhall (1985) have presented similar results from a limited survey.

Although the equipment in Room 1 was clearly operating at a lower exposure to the patient, it should be remembered that, as has been pointed out by Faulkner and Moores (1982), the radiation dose to any staff at the couch side is considerably higher for this type of equipment. The overcouch tube/undercouch intensifier configuration is designed for remote control use, but fluoroscopy must on occasions be carried out with personnel in the vicinity of the patient. During this survey, maximum use of the distance factor in staff protection was made in this circumstance.

TABLE VI

MEDIAN, 2½ AND 97½ PERCENTILES OF FLUOROSCOPIC EXPOSURE (RCM²) FOR BARIUM MEAL EXAMINATIONS USING AUTOMATIC AND MANUAL DOSE CONTROL IN ROOM 2

	No. of examinations	Median exposure (fluoroscopic)	2½ percentiles	97½
Automatic	386	820 (1020)	90	3430
Manual	507	950 (1110)	170	2810

Values in parentheses are means.

Several factors may have a bearing on the difference in radiographic exposures delivered in the two rooms. It is conceivable that fewer films were used per examination in Room 1 or that higher kilovoltages were employed resulting in lower doses, but by reference to Table V it can be seen that the differences are largely due to the regular use of the 105 mm camera with AEC, instead of film-screen cassettes. Another factor which may relate to this is the regular use of AEC for cassette films in Room 1. This is likely to have led to a reduction in the numbers of repeat films.

Table III also highlights the variations in exposures delivered by the different radiologists. Since the distributions of patient size and examination type are similar for each, it is deduced that these variations are largely attributed to the different techniques employed by individual radiologists.

It is noticeable that in Room 2, which was used by all the radiologists, those who delivered the highest fluoroscopic exposures also tended to deliver the highest radiographic exposures.

Mean screening times are shown in parenthesis in Table IV for both males and females. The National Radiological Protection Board (NRPB) (Wall et al, 1980) have quoted values for three of the examinations presented here. In comparing these it is noted that the figures for barium enemas and cystography are similar, whilst the NRPB value of 2.94 min for barium meals is somewhat less than those recorded during this study. However, the relevance of the mean value needs to be considered carefully.

From Table IV, it can also be seen that both median and mean exposures to male patients are consistently higher than to female for both the fluoroscopic and radiographic components of all the common examinations. The ratios of these are within the range 1.0 to 1.5. Since the median and mean exposure values are obtained from large numbers of patients, and the distribution of sexes amongst rooms and radiologists is unbiased, it is concluded that the consistently higher exposures to males are due entirely to the fact that the average weight of the males was greater than that of the females.

Den Boer (personal communication, 1985) has shown that patient dose and image quality are related to a parameter which he defines as "obesity index", which depends on height and weight. Patient height was not recorded during this survey, nor was patient thickness measured with calipers, but the weight of each patient had been recorded and the correlation between this and the fluoroscopic exposure rate (measured exposure divided by recorded screening time) was calculated for each of the most common examinations. No significant correlation was found for any of the examinations.

However, when the patient weights were divided into 10 kg groups, and the median (or mean) exposure rate within each group plotted on a graph, the result (Fig. 3) showed a clear trend (supported by results of a Mann-Whitney *U*-test). It is concluded that the fluoroscopic exposure rate is only related to patient weight when median (or mean) values are obtained from a large sample. The extremely wide variations in exposure rate that exist within any weight category are caused by wide variations in field size, tissue thickness and other factors over the range of examinations.

In particular, for patients of high or low weights, the exposure rate delivered is not significantly different from that delivered to a patient in the adjacent weight group. In other words, it is only at the central weight values that the system (either the radiologist/radiographer, or, in the case of automatic exposure control, the equipment) is able reliably to detect differences in patient weight and to deliver appropriate exposures. It seems likely that at the extremes of patient weights, the equipment, particularly the automatic exposure control, is reaching the limits of its capability. This became apparent in the examination of infants and young children in which manual control of fluoroscopic exposure produced a significant reduction.

Table V shows clearly the benefits which may result in terms of patient dose from using 105 mm camera films during these procedures in place of the film-screen cassette method. As with all methods of dose reduction, this should be viewed carefully, bearing in mind the trade-offs which may result from reduced image quality.

The value of automatic fluoroscopic dose control in Room 2 may be assessed by referring to Table VI. It is apparent that in this case only a small saving in exposure is achieved by using the automatic system. This suggests that, if image quality under both manual and automatic control is satisfactory but no better than necessary, the radiologists at this particular hospital are, on average, using the equipment in a dose-efficient manner. This does not necessarily mean that automatic systems are of no value. One has only to refer again to Table III to observe the exposures delivered by different radiologists. Whereas Radiologists 4 and 7 employ average fluoroscopic exposures which are significantly lower than the average exposure under automatic control, Radiologists 1 and 5 employ significantly higher average fluoroscopic exposure. Automatic control could help to reduce average screening exposures for individual radiologists.

CONCLUSION

This study has examined some of the factors influencing the fluoroscopic and radiographic radiation exposures to patients undergoing common fluoroscopic procedures.

Median and mean exposures in two rooms fitted with different types of X-ray equipment varied by a factor of two or more. The variation in fluoroscopic exposures was due to the different dose rates at which the two intensifiers were operating, and the lower radiographic exposures were associated with the use of a 105 mm camera.

The ratios between the highest and lowest median exposures given by individual radiologists are 1.7 for fluoroscopy and 2 5 for radiography. While the authors do not presume to consider what comprises a satisfactory result from a clinical point of view, there is no doubt that some radiologists conduct their examinations with lower exposures to the patient than others. Whether or not this lower exposure indicates that there is less diagnostic information is an open question. The differences in technique may involve variations in fluoroscopic exposure time, number of films taken, exposure factors used, or beam size. It cannot be stressed too often that radiation doses can be kept low not only by keeping screening time and number of films low, but also by maintaining the image quality (TV or film) at a level no higher than necessary, and imaging an area no larger than the region of clinical interest.

If any guidance is to be given in the future regarding the range of exposures which may typically be expected during specific fluoroscopic examinations, then this would obviously have to take account of many factors noted in this paper including the size of the patient. Patient weight alone has been shown to be insufficient for an accurate prediction of patient exposures. The concept of an index of obesity may prove to be of more help in relating exposure to patient size.

Radiographic exposure savings of 75% or more have been achieved during the examinations studied here by use of the 105 mm camera. Clearly this should be used regularly where the image quality resulting is likely to prove clinically satisfactory.

In this survey, an overall advantage of automatic control of fluoroscopy was not demonstrated. The results suggest that a skilful operator can achieve adequate results using manual control and in some circumstances it was manifest that an exposure to the patient significantly lower than that from an automatic system was achievable.

Finally, when assessing the purchase of new equipment in the light of the above considerations, it is essential that the inter-relationship of costs, risks and benefits to the patient, staff and community at large, be fully examined.

ACKNOWLEDGMENTS

The authors wish to thank the radiologists at Blackpool Victoria Hospital for their willing co-operation and the many radiographic and clerical staff for their efforts over a long period in recording and initial handling of the data. We also acknowledge the assistance of Mr R. Swindell, Department of Statistics, Christie Hospital, in the statistical analysis of the data

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Book reviews

Forty-five Years of Cancer Incidence in Connecticut 1935–79. NCI Monograph 70. Ed. by M. M. Cusano and J. L. Young, pp. lvii+706, 1986 (US Department of Health & Human Services, Bethesda).
NIH Publication No. 86–2653

This report covers the cancer cases registered in the State of Connecticut from 1935 to 1979. During that period 316000 cases were registered and the information from these is presented in a large number of tables, giving breakdowns by site, age, sex and period of diagnosis. There are also tables giving the percentage of cases confirmed histologically, registered from the death certificate only, and diagnosed first at autopsy. In the first quinquennium (1935–39) about a third of all registrations were obtained from the death certificate; in 1975–79, only a little over 1%. About half were confirmed histologically in 1935–39; over 90% in 1975–79. No data are provided on survival.

The report provides a rich seam for exploration by anyone interested in trends in cancer incidence. The changing patterns in cancer of the breast and cervix are very evident, as is the relative increases in cancer of the lung in males and females. Over the most recent three quinquennia, lung cancer in females has more than doubled, while rising by only a quarter in males. Many other such interesting facts are no doubt hidden in the tables, which are very well presented. A separate publication summarising some of the main trends would be valuable.

John Haybittle

Living With Radiation. National Radiological Protection Board, pp. 53, 1986 (Her Majesty's Stationery Office, London), £1.50.
ISBN 0–85951–255–X

This booklet, written anonymously by members of the staff of the National Radiological Protection Board, is a short review of the sources and effects of human exposure to ionising radiation, and the means of radiological protection. The last edition was published 5 years ago, and this new one closely follows the pattern of its predecessor. The major change from a radiologist's viewpoint is the halving of the estimate of the population radiation dose from medical procedures, this despite an increase in the number of examinations. As has been indicated by the National Radiological Protection Board, much of this decrease arises because of an earlier overestimate of the radiation dose from X-ray radiodiagnosis. The identification of a few houses delivering 0.1 Sv/year from radon decay, 100 times the average, is noted. The Chernobyl disaster is briefly recorded, obviously at a late stage in the preparation of the book. I think the section on the safety of power stations might have been rewritten in view of this accident if there had been more time.

The previous edition had large print, useful when teaching small groups. The print is smaller in this edition; in places a bright light and perhaps a magnifying glass are needed.

For many years there has been no difficulty in choosing this booklet as the one to recommend to those wanting an introduction to ionising radiation (for medical students, nurses, interested lay people) and, for oneself, as a convenient reference source for refreshing the memory and teaching. This new edition will continue to fill these roles.

J. G. B. Russell

Radiation Protection in Radiotherapy. Ed. by A. L. McKenzie, J. E. Shaw, S. K. Stephenson and P. C. R. Turner, pp. x+102, 1986 (Institute of Physical Sciences in Medicine, London), £12.50.
ISBN 0–904181–41–3

This report from the Institute of Physical Sciences in Medicine provides a good reference for those involved in radiation protection. The initial chapter includes a synopsis of the salient points of radiation protection with respect to radiotherapy. Chapters 2, 3 and 4 discuss external beam therapy, brachytherapy and therapy using unsealed radioactive sources, respectively. Each of these chapters describes both treatment and protection principles, with consideration of *The Ionising Radiations Regulations 1985*. Emergency arrangements and external and internal radiation hazards are also covered.

Chapter 5 indicates the practicalities of following the new regulations in terms of personal and environmental monitoring. Certain types of monitoring equipment are described, but not all; regulatory levels for controlled areas, derived limits and some examples of annual limits of intake are given, whereas whole-body dose limits are not. The final chapter explains the organisation and administration of a radiation protection service, indicating the necessary duties of radiation protection advisers, radiation protection supervisors and heads of departments.

Guidance in radiation protection incorporating the new regulations will be greatly appreciated. Considerations are listed which will assist those currently preparing local rules and a comprehensive list of references directs the reader towards more detailed information, when required.

The book is well prepared and formatted in a style which is helpful to the reader. Key points can be easily located without wading through the bulk of the text. Although it does not act as an introduction to the subject, it is recommended as an aid to those already involved in radiation protection.

A. P. Cameron

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The associated X-ray spectra of Amersham caesium-137 afterloading sources

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ABSTRACT

Low-energy X rays are clearly observed in the energy spectra of Amersham ^{137}Cs afterloading sources. Examination is made of the effects of encapsulation and source train attenuation on the source spectra. Estimates of the resulting X-ray intensities are also made.

The radionuclide ^{137}Cs has found widespread use as a brachytherapy source in intracavitary and interstitial treatments of cancer In this context the Amersham intracavitary ^{137}Cs afterloading system has been particularly popular (Bateman et al, 1983; Mould & Hobday, 1983). Although it is well established that 84.7% of the decay takes place through gamma emission of the 662 keV photon and a further 6.89% takes place through the associated ^{137}Ba^{m} K X-ray emission process, little attention appears to have been accorded to changes in source spectrum with encapsulation (Horsler et al, 1964; Attix, 1968, Diffey & Klevenhagen, 1975; Johns & Cunningham, 1980; Lorenz, 1983)

We report here a spectroscopic study of the relative intensities of the ^{137}Ba^{m} X ray and 662 keV photon emissions. In addition, a fluorescent component is evident in the region of 50 keV, which would appear to be the result of the particular choice of spring steel sheath that surrounds each Amersham ^{137}Cs afterloading source. From the relative intensities of these X rays, an estimation of their contribution to the overall intensity has been made.

APPARATUS AND METHODS

We have used four ^{137}Cs sources in this study.

(1) A low-activity source of 2.6 MBq. This consisted of a disc, diameter 2.5 cm, of thin fibrous absorbent material (proprietary name Benchkote, Whatman Ltd) onto which a few drops of ^{137}Cs had been added.

(2) A 444 MBq ^{137}Cs stainless-steel seed taken from an Amersham manual afterloading ovoid source. Seeds such as these consist of three active glass beads, of diameter 1.1 mm, arranged in a line and encapsulated in 316L grade stainless-steel of outer diameter 1.8 mm and length 5 mm.

(3) An 888 MBq ^{137}Cs source, taken from an Amersham manual afterloading source, consisting of two stainless-steel seeds of the same construction and dimension as detailed above. The two seeds were retained in a stainless-steel source train outer spring of outer diameter 2.6 mm (specified as 0.102 in).

(4) A 1295 MBq ^{137}Cs Amersham manual afterloading system ovoid source consisting of three seeds and a source train outer spring, all of construction and dimensions as detailed above.

Sources 2 and 3 were sealed in separate, thin-walled (nominally 1 mm), perspex plugs, allowing easier access to remote handling while minimising the possibility of loss.

Measurements were made using a shielded NaI detector, 2 mm thick, to facilitate detection of low-energy photons, and a NaI detector, 5 cm (2 in) thick, to facilitate detection of the more energetic photons. The spectra were recorded using a 1024-channel Tracor Northern MCA. Sources were positioned so as to give acceptable count rates, the position of each source being noted in order to allow subsequent comparison of the 662 keV photon full-energy-peak intensities. In addition to the NaI detectors, a Ge(Li) detection system was also used, in order to allow closer examination of the fluorescent component. It is to be noted that although the efficiency of the Ge(Li) is somewhat limited at low energies, it nevertheless remained sufficiently good to allow study of the individual fluorescence X-ray lines involved.

RESULTS AND DISCUSSION

Spectra

Figure 1 shows the low-energy spectra ($E < 100$ keV) for all but the 888 MBq source, which provided a spectrum not significantly different from the 1295 MBq source. For energies in the range 70–800 keV spectra for only the 2.6 MBq and 888 MBq sources have been included. In the case of the low-energy spectra, one is able to identify not only the Ba K X radiation in the region of 35 keV (tabulated values indicate that Ba K_{α} and K_{β} fluorescence are to be found at 32.062 keV and 36 354 keV, respectively) but also fluorescence peaks at approximately 8 keV and 80 keV. The 8 keV peak is due to Fe fluorescence and arises predominantly from the interaction of the 662 keV photon, with the steel encapsulation of each of the three higher-activity sources; tabulated values show Fe, K_{α} and K_{β} fluorescence to be at 6.398 keV and 7 057 keV, respec-

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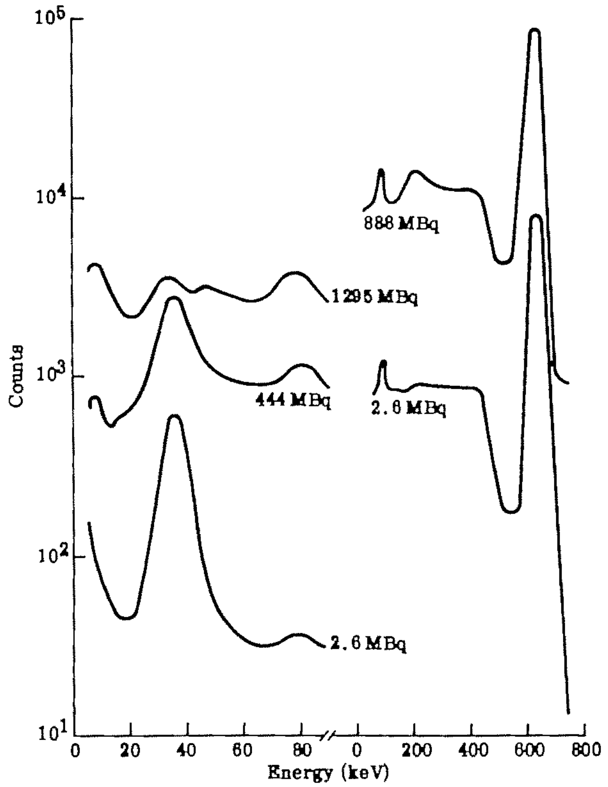

Fig. 1

Spectrum of variously attenuated ^{137}Cs sources; the two energy regions illustrated are $E < 100$ keV and $E < 800$ keV.

tively. The 80 keV peak is, on the other hand, due to Pb fluorescence arising from the interaction of the 662 keV photon with the detector shielding arrangement; tabulated values show Pb K_α and K_β fluorescence to be at 74.221 keV and 84.859 keV, respectively. Only in the case of the 888 MBq and 1295 MBq sources is an additional peak evident in the region of 50 keV. Since only the two most active sources have a stainless-steel spring sheath, the basis of the peak most probably lies in the composition of the steel spring itself; this might differ from that of the stainless-steel encapsulation of each of the ^{137}Cs seeds since there is no such obvious component for the 444 MBq bare seed source A more detailed investigation of the energy region has been performed using a Ge(Li) detector. From the position of the X-ray lines, and bearing in mind the stainless-steel grades that could possibly have been used to form the spring, the indication is that one is seeing Ta fluorescence (although 316L does not contain Ta, the closely related grades 347 and 348 do).

The Ge(Li) detector was also used to investigate the intensity of the ^{134}Cs contaminant generally associated with ^{137}Cs. No measurable contamination was found at 794 keV.

Analysis has been made of the various peak areas and, based on this, normalisation of the 1295 MBq, 888 MBq and 2.6 MBq sources to the actual activity of the nominal 444 MBq source (known from the Amersham test certificate to within 5%) has been undertaken utilising the 662 keV peak. Agreement with the known activities of the other sources has been obtained, in each case, to within 5%. Ratios of the peak areas obtained in the region of 35 keV to those obtained at 662 keV have also been calculated. The results, normalised to the unattenuated 2.6 MBq source, are provided in Table I; as 6.89% of the total radiation intensity is attributed to the $^{137}Ba^m$ X-ray emission, these results are actually expressed as the fractional intensities provided by the attenuated $^{137}Ba^m$ X-ray peaks obtained for the 1295 MBq, 888 MBq and 444 MBq sources.

The expected reduction in intensity of the $^{137}Ba^m$ X-ray peaks has also been calculated based on the attenuation coefficients of Hubbell (1982). In this respect, recent absorptiometric studies of biomedically interesting substances, using the ^{137}Ba X rays, have

TABLE I

Values of intensity reduction (I/I_0) for the three variously encapsulated ^{137}Cs sources under study

Source description and associated activity	Reduction in intensity I/I_0*		Contribution‡ to overall intensity (%) based on present measurement
	Hubbell (1982)†	Present measurement	
Single ^{137}Cs seed (no additional encapsulation) 444 MBq	0 22	0.234	1.64
Two ^{137}Cs seeds retained in stainless-steel spring 888 MBq	0 05	0.076	0 53
Complete Amersham intracavitary ^{137}Cs afterloading system ovoid source in stainless-steel spring. 1295 MBq	0.05	0.063	0.44

*(I/I_0) represents the ratio of attenuated (I) to unattenuated (I_0) intensity

†Estimates of intensity reduction on the basis of the tabulated mass attenuation coefficients of Hubbell (1982) and the attenuating thickness involved.

‡Arising from Ba K X-ray fluorescence and where applicable, fluorescence arising from the stainless-steel spring.

shown that an effective energy of 33 keV can be taken as being representative of the X-ray spectrum (Bradley et al, 1985a,b; 1986) The results show that for a ^{137}Cs seed encapsulated in 0.3 mm-thick stainless steel, the reduction in intensity is approximately 0 22, whereas with the addition of a stainless-steel spring of additional thickness of 0.3 mm, the value is approximately 0 05 (where μ_{Fe} at 33 keV is taken to be 50 cm^{-1}). It is to be noted that, although there is general agreement with the measured intensities, these values are only to be taken as estimates; among other uncertainties are the values chosen for steel thicknesses, these being nominal. Account has not been taken of self-attenuation within the ^{137}Cs glass-bead sources at 33 keV or of the relatively small attenuation, of the order of 2.8% (Amersham International plc, 1978), of the 662 keV photons.

It is also to be noted that the measurements on which the tabulated results are based were for configurations in which the long axes of the source seeds were normal to the line joining source to detector. Oblique filtration effects were, therefore, taken to be minimal. Measurements undertaken with the source seeds in an end-on configuration display the expected characteristic reduction in intensity.

Since the fluorescence X-ray peak is observed to be only slightly lower in intensity when compared with the 33 keV component and since the attenuation of 50 keV photons is somewhat less than that at 33 keV, then it is expected that the fluorescence X rays provide a comparable contribution to the overall intensity

CONCLUSION

Spectral study of encapsulated Amersham ^{137}Cs afterloading system sources reveals that ^{137}Ba^{m} and fluorescence X-ray peaks are in evidence. Encapsulation of these sources results in an overall reduction in intensity of the ^{137}Ba^{m} X-ray component from 7% of the total intensity to approximately 1 6%; with the additional attenuation provided by a stainless-steel spring, the intensity contribution is reduced to approximately 0.5%. Fluorescence from the spring material evidently yields a further contribution of the order of 0.5%. It has long been realised, using available tabulated attenuation coefficients, that low-energy X-ray components provide little contribution to the overall intensity; however, in this study corroborative empirical evidence has been obtained providing quantification of the intensity of these X rays

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Book reviews

Endometrial Cancers. Fifth Cancer Research Workshop, Grenoble 1985. Ed. by M. Bolla, C Racinet and C. Vrousos, pp. x+270, 1986 (S. Karger AG, Basel), £58.10.
ISBN 3-8055-4211-9

This is a relatively short and well produced book which includes papers presented at a cancer workshop held in Grenoble in 1985 Although published in English, the majority of contributors were French and they represented both major and minor centres from that country. There is some support from surrounding countries and North America. The book covers epidemiology, detection, pathology, prognostic factors, steroid receptors and therapeutic modalities in 267 pages, with papers of very variable length. Some represent overviews of the subject while others are short reports of individual experience.

Within this framework it would be impossible to expect an account containing significant original work or detailed results There are certainly important essays on replacement therapy in the aetiology of endometrial cancer (Mack), prevention and detection (Gusberg) and prognostic factors (Bona). There are also overviews of different therapeutic approaches, including surgery and radiotherapy. The book is rather expensive and, in a large hospital library, a browser might be stimulated to pursue one of the subjects covered in the text. The experienced gynaecologist or oncologist would have to work hard to find the useful parts of this book and could, I suspect, find fuller and more satisfactory reviews more quickly elsewhere

R. D. HUNTER

Fourth Symposium on Epidemiology and Cancer Registries in the Pacific Basin NCI Monograph 69, pp. v+273, 1985 (US Department of Health and Human Services, Bethesda), NIH Publication No. 85-2768

Relatively few published data are available for many of the countries in the Pacific Basin (as defined by the NCI) and, therefore, it is an advantage to have a bound collection of papers from this area. They form the proceedings of a symposium held in Hawaii in January 1984, and many of the papers have been written by authors from the People's Republic of China. Titles of the six sections in this monograph are: "United States–People's Republic of China Co-operation in Cancer Research", "Cancer Incidence among Ethnic Populations in Different Areas of the Pacific Basin", "Progress in Cancer Research in the Pacific Basin", "Cancer Related to Occupation and Radiation Exposure", "Cross-cultural Comparisons" and "Chemoprevention Trials".

The few papers on cancer related to radiation exposure will be of more interest to BIR members than some of the other contents and there is one contribution from the University of Southern California entitled "Medical and Dental X-rays as Risk Factors for Recently Diagnosed Tumours of the Head".

The monograph will be a useful addition to the libraries of cancer registries, departments of community medicine, and large medical libraries, but will not be purchased by individuals unless they are mainly working in the field of cancer epidemiology.

RICHARD F MOULD

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Technical notes

Scattered radiation reaching doors and windows of diagnostic X-ray rooms

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(*Received April 1986*)

Areas adjacent to diagnostic X-ray departments may need to be identified as Controlled or Supervised Areas under the Ionising Radiations Regulations 1985. To assist in identifying such areas in hospitals in two Scottish Areas (Lothian and Fife), dose monitors have been placed in various sites in diagnostic X-ray rooms for at least 6 months of 1985. The sites chosen were mainly (a) X-ray room windows to areas which could be occupied, such as car parks and gardens, and (b) X-ray room doors having no lead (or an uncertain quantity) and opening onto corridors, circulating areas or waiting areas All sites chosen received scattered radiation only, except for two which were behind chest stands.

Fifty-seven sites were monitored in 30 X-ray rooms in 17 different hospitals. The majority of the rooms were general-purpose, but a number of more specialised rooms were included The hospitals ranged from a large teaching hospital to small local hospitals and clinics, and are believed to represent a reasonable sample of current UK usage and practice. A classification of the rooms and sites is given in Table I.

The dose monitors were film badges supplied and assessed by the National Radiological Protection Board (NRPB). They were exposed in ordinary holders and changed every 4 weeks for at least six periods.

Some sites gave consistent results from period to period (*e.g.* five periods giving 0.4 mSv and one giving 0.3 mSv), while others fluctuated rather more. However, the highest recorded dose at any site did not reach three times the average dose for that site In several cases doses were reported by NRPB as "soft X ray". The annual doses for all the sites are given in histogram form in Fig. 1.

Mean annual doses for each class of site are given in Table I, but no important differences between types of room or types of hospital are shown by this analysis. There are too few records for several of the subgroups of rooms.

In every case the results are satisfactorily low in that they indicate annual doses to the sites concerned of less than 15 mSv, the dose at which staff need to be classified or controlled areas need to be identified. The majority fall below an annual dose of 5 mSv, the public dose limit and the limit for supervised areas. Thus, to comply with the letter of the Regulations, no structural

TABLE I

MEAN ANNUAL DOSES IN DIAGNOSTIC X-RAY ROOMS AT 57 MONITORED SITES

	No of rooms	No. of sites	Mean annual dose (mSv)
Teaching hospital			
Fluoroscopic room	2	2	5.7
Radiographic room	4	7	3.1
District general hospital			
Fluoroscopic room	—	—	—
Radiographic room	3	6	4.8
Small hospital			
Fluoroscopic room	7	12	4.2
Radiographic room	6	11	4.6
Specialist hospital			
Orthopaedic	3	8	4.0
Paediatric	3	7	2.6
Health centre (radiographic only)	2	4	3.9

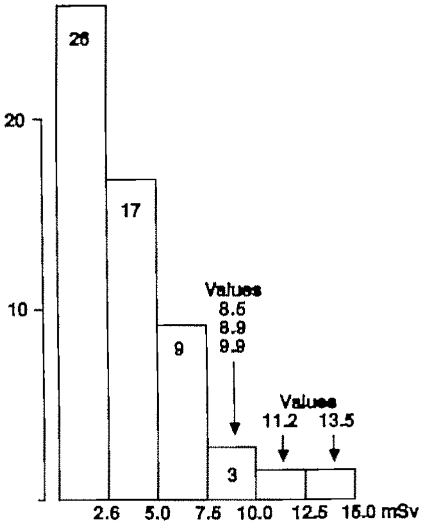

FIG. 1.

Annual doses in diagnostic X-ray rooms at 57 monitored sites (scattered radiation only) changes are necessary in any of these sites. The two highest results both come from the same room, where a large number of chest radiographs are taken each day at a skin dose of 0.1–0.2 mSv each. The highest reading was at a window behind the chest stand and, if occupancy just outside this window was significant, added protection would be recommended. The window, however, looks onto a grassed area and actual occupancy is low, *i.e.* much less than one hour in any eight, and also very infrequent.

Before drawing any general conclusions, it is necessary to consider whether the 57 sites monitored represent positions receiving less scatter than the general level in the rooms concerned. Since they have no lead at present, they must have been thought in the past not to need it, but that judgement may have been made a long time ago. Some of them have probably had no structural change made in 30 years, and, until the Regulations came into force, radiation protection advisers were expected to use their discretion in judging protection needs in places of low occupancy. From a knowledge of the sites, it seems unlikely that the doses are much below the general level for scatter in the rooms concerned.

The question then arises, is protection of conventional diagnostic X-ray rooms still necessary to the same degree as in the past? The same point might be expressed in an alternative form: even when the physical structure of a diagnostic X-ray room can be shown to achieve compliance with the Ionising Radiations Regulations (Her Majesty's Stationery Office (HMSO), 1985), is additional structural shielding nevertheless desirable, on the "as low as reasonably achievable" (ALARA) principle and, if so, then how much? X-ray room protection is still apt to be 2 mm lead equivalence, in the form of lead ply, lead glass or barium plaster, and is widely applied in protective screens for operators, on doors, and on walls or other structures having less than 9 in (23 cm) of solid brickwork. In total, it represents significant expenditure. X-ray doses may well have decreased in the last 25 years or so as a result of greater awareness of the importance of radiation protection, possibly stimulated by the Adrian Report (HMSO, 1960). Films and screens are becoming faster and, possibly, X-ray beams are better collimated than before.

In discussing this issue, perhaps the strongest argument is that complete room protection at about 2 mm lead equivalence enables the user to change subsequent use, technique or layout in that room without being constrained by possible protection problems outside the room. Layout changes can extend to a radical change in primary-beam direction, for example, possibly without the need for Local Rules to restrict beam direction. In the particular case of a very small room, the scatter to doors and windows is still likely to reach significantly greater levels than these, unless the workload is very low.

However, while the ALARA principle does require us to reduce doses where we reasonably can, it also says "social and economic factors being taken into account". A thorough discussion of this point for the sites concerned probably requires application of cost–benefit analysis, as outlined by NRPB in recent reports (NRPB, 1981, 1982). If we assume that for the X-ray room doors some person is just outside for not more than 10% of the working day (not necessarily the same individual), then over 10 years the collective dose in man-sieverts equals the annual dose. Moreover, it is received at low levels of individual dose, below 5 mSv per annum. For 10 man-mSv, NRPB (1982) suggests a "cost" of £40 when protecting radiation workers. The cost of adding lead to doors, including strengthening hinges and door posts, is likely to be in the region of £400 to £1000 per doorway, so that the benefit is not thought to justify the cost.

For windows, occupancy and, hence, the collective dose saved are likely to be much less, for example occasional gardening, patients sitting out on sunny days, or a driver in a parked car. An occupancy of around 1% is more reasonable than 10%. For protection of the public, at individual annual dose levels of 50–500 μSv, NRPB recommends a cost for 1 man-mSv of £10, so that again the benefit does not justify the cost of fitting lead ply. This leaves out any consideration of detriment from heavier doors or smaller windows.

In conclusion, scattered dose levels in diagnostic X-ray rooms appear to be lower than is often supposed, or implied by past practice in radiation protection. Rooms with previously unprotected doors or windows can probably remain unchanged. In planning new installations, significantly less than 2 mm lead equivalence all round may be entirely adequate now, but the inconvenience of adding shielding later to cope with possible change of use must be considered.

ACKNOWLEDGMENTS

The co-operation of the Superintendent Radiographers and Radiological Safety Officers in all the Departments concerned is gratefully acknowledged. I must also thank Miss A M Grant for compiling the results.

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1987, *The British Journal of Radiology*, *60*, 181–183 FEBRUARY 1987

Technical notes

A minimum data input computer program for Selectron treatment calculation

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(*Received May 1986 and in revised form August 1986*)

Several years ago in Glasgow a computer program was implemented to speed up the calculation of radiation doses given by *Selectron caesium sources to predetermined anatomical points in treatment of cancer of the cervix. The object of the program was to reduce data input to a minimum, to allow user interaction with the positioning of the active sources and treatment times and to produce the results in the standard format required for medical purposes.

Reconstruction of the three-dimensional co-ordinates of radioactive sources, using stereo or orthogonal films of an implant, is a well established procedure in many intracavitary/interstitial computer calculations. Although the standard Glasgow implant program could equally well be applied to calculation of sources in the Selectron applicators, the difficulty of locating on a radiograph the active sources within the metal applicator when *in situ* often proved to be a problem. The method described below allows the positioning of all 48 possible sources within the applicator with a minimum of data input.

GLASGOW SELECTRON CALCULATION

Treatment by Selectron is based on the Manchester system of treatment of the cervix by radium, with the central G-tubes being replaced by a curved Selectron applicator and the ovoids by the straight-line section of rigid applicators. The central applicator is shaped as shown in Fig 1, with different curvatures being available to suit patient anatomy. Likewise, ovoid applicators are available with varying degrees of bending below the straight section at the tip. All applicators are used with a mixture of 48 dummy or active sources, but since the active sources used in an ovoid-applicator never extend beyond the straight section, the shape of the stem of the ovoid applicator is immaterial to the calculation.

The points of interest at which doses are required are generated either automatically (A- and B-points) or semi-automatically (O-points), or are digitised from corresponding positions on both radiographs. A-points are defined to be 2 cm lateral and B-points 5 cm lateral from a point, P, situated 2 cm up from the end of the cervical canal. By referencing point P as a source number or a digitised point, the co-ordinates of the A- and B-points are automatically generated. Since positioning of the O-points on radiographs requires pre-knowledge of the magnification, suitable anatomical points (viz on the antero-posterior (AP) radiograph the intersection of the tangent to the femoral heads and the pelvic wall and at the depth of point P on the lateral radiograph) are first digitised. The program, after demagnifying the co-ordinates, moves their position 1 cm towards the patient's midline, thus producing the O-points. Provision has been made for an additional 13 normal digitised points identifiable on both radiographs.

The program could easily be modified to suit other pre-set points or additional digitised point data.

CENTRAL APPLICATOR DATA PREPARATION

Glasgow currently possesses 30 central applicators which, when grouped into sets of similar curvature, result in the six possible types identifiable by the program.

One applicator from each type was placed flat on an X-ray film and an unmagnified radiograph produced from which, for all six types, the parameters required to describe an applicator were generated or measured as described below.

CALCULATION METHOD

The tip of the applicator is defined as the point where the line along the centre of the applicator cuts the exterior hemispherical end This point is taken as the origin of the axes.

The curved section of the applicator from tip to F in Fig 1 can be represented accurately by the polynomial

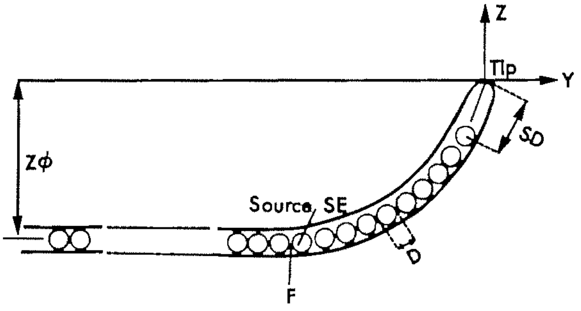

FIG. 1.

Diagram of the curved Selectron applicator and caesium ovoids

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*Nucletron Engineering BV, The Netherlands.

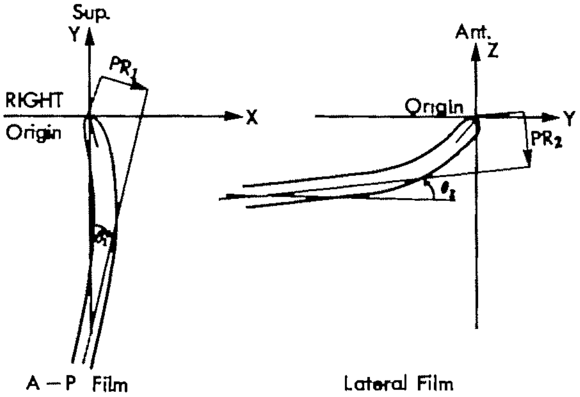
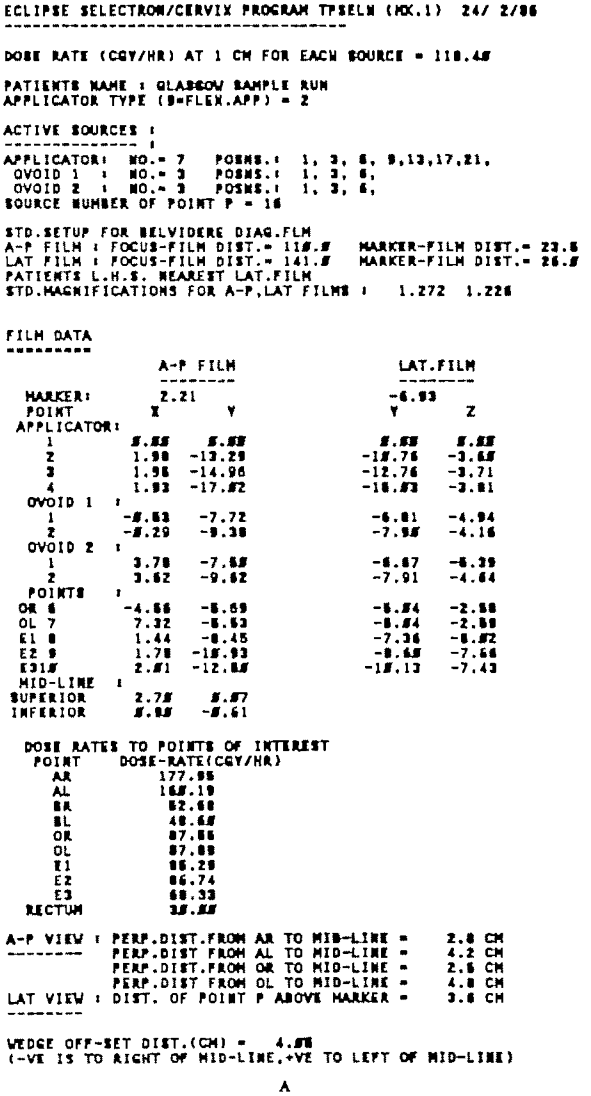


FIG. 2

Orthogonal views of the Selectron applicator.



```
ECLIPSE SELECTRON/CERVIX PROGRAM TPSELN (MK.1)  24/ 2/86
-------------------------------------

DOSE RATE (CGY/HR) AT 1 CM FOR EACH SOURCE = 118.40

PATIENTS NAME : GLASGOW SAMPLE RUN
APPLICATOR TYPE (9=FLEX.APP) = 2

ACTIVE SOURCES :
-------------- :
APPLICATOR:  NO.= 7   POSNS.:  1, 3, 5, 9,13,17,21,
 OVOID 1  :  NO.= 3   POSNS.:  1, 3, 5,
 OVOID 2  :  NO.= 3   POSNS.:  1, 3, 5,
SOURCE NUMBER OF POINT P = 15

STD.SETUP FOR BELVIDERE DIAG.FLM
A-P FILM : FOCUS-FILM DIST.= 110.0   MARKER-FILM DIST.= 23.5
LAT FILM : FOCUS-FILM DIST.= 141.0   MARKER-FILM DIST.= 26.0
PATIENTS L.H.S. NEAREST LAT.FILM
STD.MAGNIFICATIONS FOR A-P,LAT FILMS :   1.272  1.226

FILM DATA
---------
                 A-P FILM                  LAT.FILM
                 --------                  --------
  MARKER:        2.21                     -6.93
  POINT          X       Y                 Y        Z
 APPLICATOR:
    1          0.00    0.00              0.00     0.00
    2          1.90  -13.29            -10.76    -3.60
    3          1.95  -14.96            -12.76    -3.71
    4          1.93  -17.02            -15.03    -3.81
  OVOID 1   :
    1         -0.53   -7.72             -6.81    -4.94
    2         -0.29   -9.38             -7.90    -4.16
  OVOID 2   :
    1          3.78   -7.50             -6.67    -5.39
    2          3.62   -9.02             -7.91    -4.64
  POINTS    :
 OR 6         -4.55   -5.69             -5.04    -2.58
 OL 7          7.32   -5.53             -5.04    -2.59
 E1 8          1.44   -8.45             -7.36    -6.02
 E2 9          1.78  -10.93             -8.60    -7.66
 E310          2.01  -12.00            -10.13    -7.43
  MID-LINE  :
 SUPERIOR      2.70    0.07
 INFERIOR      0.90   -0.61

  DOSE RATES TO POINTS OF INTEREST
   POINT     DOSE-RATE(CGY/HR)
     AR          177.95
     AL          160.19
     BR           52.68
     BL           48.60
     OR           87.55
     OL           87.89
     E1           95.29
     E2           86.74
     E3           68.33
   RECTUM         30.00

A-P VIEW : PERP.DIST.FROM AR TO MID-LINE =    2.8 CM
--------   PERP.DIST FROM AL TO MID-LINE =    4.2 CM
           PERP.DIST.FROM OR TO MID-LINE =    2.5 CM
           PERP.DIST FROM OL TO MID-LINE =    4.8 CM
LAT VIEW : DIST. OF POINT P ABOVE MARKER =    3.8 CM
--------

WEDGE OFF-SET DIST.(CM) =   4.06
(-VE IS TO RIGHT OF MID-LINE,+VE TO LEFT OF MID-LINE)
```

A

$y = A + Bz + Cz^2$. From the radiograph of the applicator, using co-ordinates of selected points along the curved section, the parameters A, B and C were calculated using a polynomial curve-fitting program.

All 48 source positions can be computed using the following measured and calculated parameters, illustrated in Fig. 1.

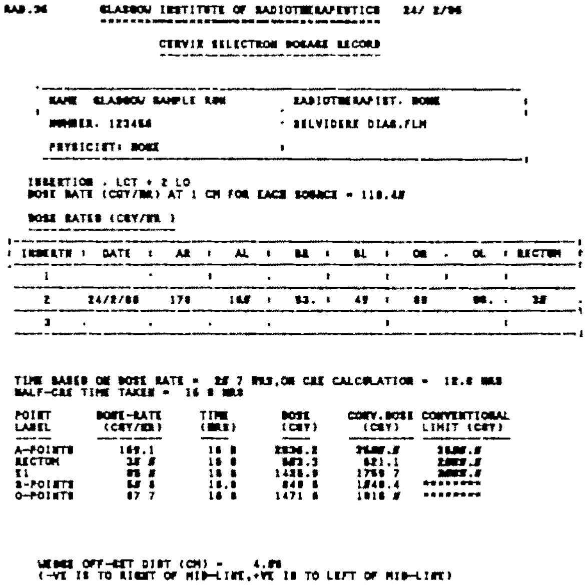
(1) Source diameter, D.
(2) Distance from the tip of the applicator to the centre of the first source, SD.
(3) Projection of the tip of the applicator to the stem line, $Z0$.
(4) Polynomial parameters A, B and C, described above.
(5) The source number where curvature ends, SE.

The problem remaining is to rotate and tilt the applicator into the matching position within the patient.

Figure 2 illustrates orthogonal views of the applicator. On the AP radiograph the tilt to the patient's right or left is angle θ_1 and on the lateral radiograph the tilt anterior or posterior is θ_2.

θ_1 is the angle between the y-axis and the line joining any two points on the straight stem of the applicator (subsequently referred to as the stem-line); likewise, θ_2 is the angle between the y-axis and the stem-line.

The degree of rotation of the tip of the applicator can be calculated from the projection distance, PR_1 or PR_2, of the tip onto the stem-line and the known true projection distance $Z0$.



```
RAD.36       GLASGOW INSTITUTE OF RADIOTHERAPEUTICS   24/ 2/86
             ----------------------------------------

                    CERVIX SELECTRON DOSAGE RECORD
                    ------------------------------

   .-----------------------------------------------------------.
     NAME  GLASGOW SAMPLE RUN          RADIOTHERAPIST. NONE      :
   :                                 .                           :
     NUMBER. 123456                  . BELVIDERE DIAG.FLM
     PHYSICIST: NONE                 :
    -----------------------------------------------------------:

  INSERTION . LCT + 2 LO
  DOSE RATE (CGY/HR) AT 1 CM FOR EACH SOURCE = 118.40

  DOSE RATES (CGY/HR )
  --------------------
:-----------------------------------------------------------------------:
: INSERTN : DATE  :  AR  :  AL  :  BR  :  BL  :  OR  .  OL  : RECTUM  :
.-----------------------------------------------------------------------:
     1          .      :      .      :      :      :      :
 ----------------------------------------------------------------------
     2    24/2/86    178     160  :  53.  :  49  :  88      88. .   30   .
 ----------------------------------------------------------------------:
     3  .       .      .      .                   :            :
 ----------------------------------------------------------------------:


TIME BASED ON DOSE RATE =  2[illegible] 7 HRS,ON CRE CALCULATION =  12.8 HRS
HALF-CRE TIME TAKEN =  16 8 HRS

POINT        DOSE-RATE     TIME      DOSE      CONV.DOSE CONVENTIONAL
LABEL         (CGY/HR)     (HRS)     (CGY)       (CGY)   LIMIT (CGY)
-----        ---------     -----     -----     --------- ------------
A-POINTS       169.1        16 8     2836.2    [illegible]   [illegible]
RECTUM          30 0        16 8      503.3      621.1     [illegible]
E1              85 0        16 8     1428.9     1759 7     [illegible]
B-POINTS        50 6        16.8      840 6     1040.4     ********
O-POINTS        87 7        16 8     1471 6     1816 0     ********


     WEDGE OFF-SET DIST (CM) -    4.06
     (-VE IS TO RIGHT OF MID-LINE,+VE IS TO LEFT OF MID-LINE)
```

B

FIG. 3.

(A) A sample of the computer output, (B) final form presented.

COMPUTER PROGRAM INPUT DATA

The keyboard information required by the program is as follows.

(1) Dose rate (cGy/h) 1 cm from each source.
(2) Type of curved applicator (this identifies the applicator parameters).
(3) Number of straight-line applicators.
(4) For each applicator, the number of active sources and their position number (1–48 for the central applicator, 1–15 for the others).
(5) Specification of point P—digitised point or source number.
(6) The number of extra points to be calculated (additional to A-, B- and O-points).

Digitised data are taken from orthogonal radiographs positioned on the digitiser as shown in Fig. 2. The digitised points on each film are as follows.

(1) Marker, used to calculate the film magnification
(2) The tip of the curved applicator, used to define the origin.
(3) Three arbitrary points along the stem-line. (These points are used to generate the tilt angles only, therefore they need not correspond on both radiographs. The points are used in pairs and the tilt angle is taken as the average of the resulting three angles.)
(4) The tip and one point along the stem of any straight-line applicator
(5) Point P (if not a source number).
(6) O-points and any additional anatomical points (such as rectal marker).

Calculation then proceeds by computing the 48 source positions of the central applicator and 15 source positions of the straight-line applicators. The digitised points are demagnified and the rotation and tilt angles computed and applied to the source co-ordinates. By calculating the distance from each active source to a point of interest and applying the inverse-square law to the source activity, the dose rate per source is computed and accumulated for all active sources. Oblique filtration and tissue absorption factors are ignored.

ENHANCEMENTS TO THE PROGRAM

A number of options have been added to the basic program described above.

(1) Repeat calculation by changing the number of active sources and their position.
(2) The offset position, relative to midline at the level of point P, of any shielding block to be used with external beam therapy.
(3) An interactive biological correction for acute effects, based on an input CRE level for A-points and tolerance levels on rectum or any other vulnerable area.

COMPUTER DETAILS

A sample of the computer output and the final form presented are shown in Fig. 3.

The program is written in Fortran and is currently running on a PDP 8/A computer, a Data General NOVA 1200 computer and on the Eclipse computer of an IGE/RTPLAN system.

Book review

Radiologic Atlas of Rheumatic Diseases. By Wolfgang Dihlmann, pp. 383, 1986 (Georg Thieme Verlag, Stuttgart), DM248.
ISBN 0-86577-237-1

This atlas is derived from the author's very extensive experience in rheumatological radiology and reflects the many important original contributions he has made to the subject The introductory sections provide a general appraisal of the radiological signs in rheumatic diseases, as well as stressing the relative merits of various radiographic techniques and other imaging methods Subsequent sections are devoted to rheumatoid arthritis, seronegative spondylarthritis, the classic collagen diseases, the enthesopathies and, finally, gout and pseudogout. A brief description of the clinicopathological background to each disorder precedes the illustrations. The terminology is generally that in common usage within the United Kingdom.

The illustrations are, to the credit of the publishers, large and uniformly superb in quality. The captions are fully descriptive and clearly emphasise areas of diagnostic importance and difficulty, with the free use of markers to highlight particular points Another strength of the book is the liberal inclusion of radiographs illustrating differential diagnoses alongside those of particular diseases. The need for careful radiological observation is reiterated throughout the book Among the many attractive features, the description of sacroiliitis is a masterly presentation.

Illustration of the extra-articular manifestations of rheumatic diseases would have made the book even more comprehensive in its content. For instance, the thoracic manifestations of rheumatoid arthritis and the gastrointestinal features of systemic sclerosis receive only scant attention. There is no coverage of the cardiac and respiratory tract in ankylosing spondylitis and systemic sclerosis, or of the arteriographic features in polyarteritis nodosa. Expansion of the section on crystal arthropathies, apart from gout, and the inclusion of a separate section dealing with osteoarthritis would have been advantageous.

Despite these criticisms, this atlas fills a niche in the radiological literature. It is recommended as a reference source for all X-ray departments concerned with rheumatology and for the radiologist with a special interest in the subject. Trainee radiologists will find it a useful review of the subject and one which includes many important points not covered in the general radiological literature.

G. H. WHITEHOUSE

1987, *The British Journal of Radiology*, *60*, 185–188 FEBRUARY 1987

Case reports

Massive intracranial pannus and a pseudomeningocoele in the atlanto-dental interval in rheumatoid arthritis

By J. M. Stevens, M.R.A.C.R., F.R.C.R., Sue Barter, M.R.C.P., F.R.C.R. and B. E. Kendall, F.R.C.P., F.R.C.R.

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(*Received February 1986*)

The joints in the region of the cranio-vertebral junction have been estimated to be involved radiologically in 19–36% of patients with chronic, deforming rheumatoid arthritis (Sharp & Purser, 1961; Stevens et al, 1971; Matthews, 1974). Eulderink and Meders (1975) reported that pathological evidence of involvement of the cervical spine was found in 59% of 44 cases at autopsy, and in over 70% of these the joints of the cranio-vertebral junction were affected. Existing literature emphasises the clinical significance of subluxation rather than of associated granulation tissue. Nevertheless, it has been shown on computed myelo-cisternography that pannus is frequently the dominant factor responsible for the actual configuration of compressive deformity of the spinal cord near the foramen magnum (Stevens et al, 1986), though the clinical importance of this observation has been denied by others (Laasonen et al, 1985) This is a report of a case which showed two distinctly unusual features: a huge intracranial mass of rheumatoid granulation tissue, most probably of synovial origin, causing brain-stem compression, and a pseudomeningocoele prolapsing into the atlanto-dental interval when the neck was flexed.

CASE REPORT

Mrs D. B, aged 65 years, suffered from progressively deforming rheumatoid arthritis for over 30 years. The disease had been complicated by neutropenia in the past 3 years and the patient was known to have mild hepato-splenomegaly. Three months previously she had noticed progressive weakness in the arms and legs, then, suddenly, 8 days before admission she felt her neck "give way", and experienced severe neck pain radiating between her shoulders. Subsequently, attempted neck movement would often result in shooting pains radiating into all four limbs. On examination she had marked proximal muscle wasting, but also brisk reflexes and equivocal extensor plantar responses. She was considered to have myopathy, probably related to prolonged glucocorticoid therapy, and also to have involvement of the descending motor tracts, probably originating from cord compression at the cranio-vertebral junction

Plain radiographs showed marked atlanto-axial subluxation. A conventional water-soluble myelogram was performed, the contrast medium being introduced by lumbar puncture. Only limited radiography was possible because of the painful arthritis There was a reducible atlanto-axial subluxation and a dense collection of contrast medium was shown lying between the dens and the anterior arch of the atlas when the neck was flexed Computed myelo-cisternography performed within 1 h of the myelogram showed a large, lobulated soft-tissue mass in the ponto-medullary cistern, and free filling with contrast medium from the subarachnoid space of the widened atlanto-dental interval with neck flexion, and emptying when the space was reduced on extension. In addition, there was marked compression of the first cervical segment of the spinal cord by the dens and posterior arch of the atlas.

One week later a transoral odontoidectomy was performed. Abundant pannus was encountered, and the material accessible from the exposure was cautiously removed The operation was carried out with the neck in extension and the subarachnoid space was not entered. At the same operation, a posterior fusion was performed with fixation by occipito-atlanto-axial interlaminar wiring. Material sent for histological examination was reported as connective tissue showing chronic inflammatory changes, consistent with pannus.

The patient had a stormy post-operative course complicated by urinary tract infection, pyelonephritis and septicaemia. However, she showed both subjective and objective increase in power in all limbs, especially the legs, and was discharged in reasonable health but requiring further rehabilitation. The pharyngeal wound healed well and at no stage was there any leakage of cerebrospinal fluid.

DISCUSSION

Clinical involvement of the central nervous system in rheumatoid arthritis is relatively common in patients with long-standing disease. Stevens et al (1971) found evidence of myelopathy in 24 of 36 patients with radiological changes at the cranio-vertebral junction, though others have reported a considerably lower incidence (Redlund-Johnell, 1984). The mechanism of involvement has almost always been reported as compression, usually from subluxation but also from thickening of the soft tissues (pannus), pathological fracture, spontaneous epidural haemorrhage, or sequestrated disc material in combination with pannus (Hopkins, 1967). Other mechanisms which have been reported include compression or thrombosis of the vertebral arteries (Webb et al, 1968; Crellin et al, 1970), angiitis of small and medium-sized arteries, and there has been at least one report of a form of amyloid

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Address for correspondence: Dr J. M. Stevens, The National Hospitals for Nervous Diseases, Maida Vale, London W9 1TL.

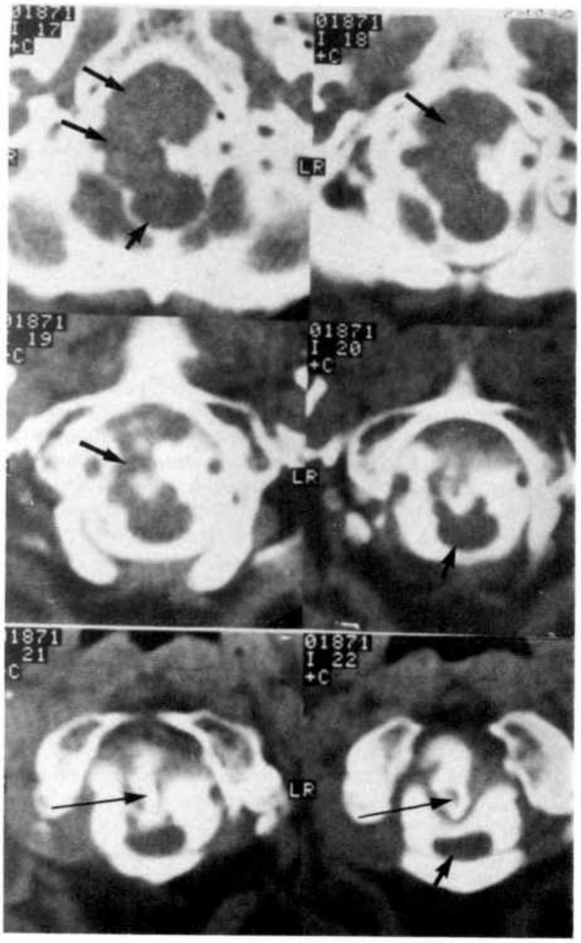

FIG. 1.

A set of six sequentially descending axial images from the computed myelo-cisternogram. These show compression and distortion of the lower part of the medulla oblongata (short arrows) by a large soft-tissue mass (longer arrows) which is in continuity below with the displaced tip of the dens (very long arrow). Severe compression of the first segment of the spinal cord (short arrows) by the dens is also shown.

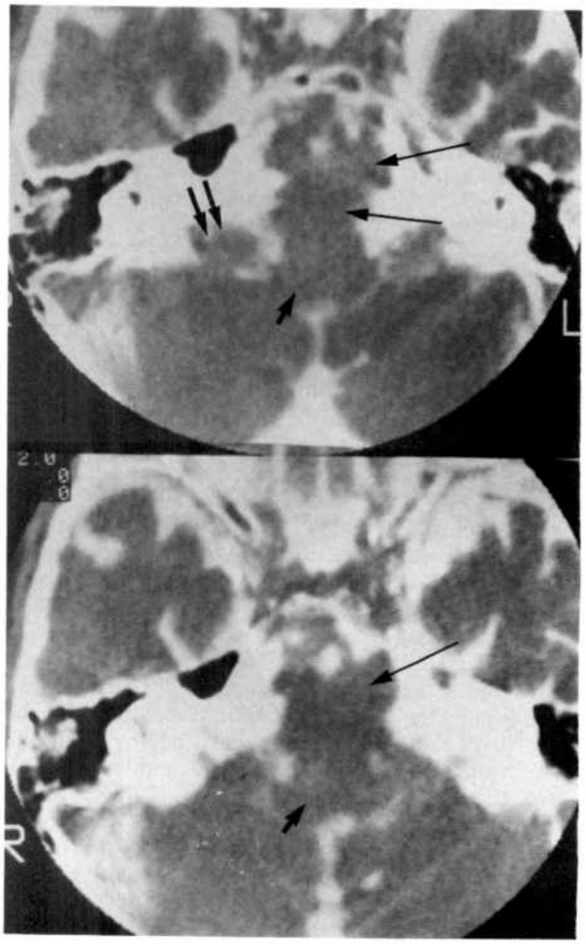

FIG. 2.

Axial images showing the upper part of the mass occupying the anterior medullary cistern where it most resembled an epidermoid tumour. Short arrows, upper part of the medulla oblongata; double arrows, flocculus; long arrows, the mass. The lower image includes the ponto-medullary junction.

angiopathy showing subarachnoid and subdural haemorrhage and widespread ischaemic encephalomalacia (Steiner & Gelbloom, 1959).

Extra-articular rheumatoid nodules have been described in the intracranial dura mater by several pathologists, though they have not been a cause of neurological dysfunction (Ellman et al, 1954; Maher, 1954; Steiner & Gelbloom, 1959). These lesions were studded over the dura of the cranial vault as well as in the skull base. The largest individual nodule was 1.5 cm × 1.4 cm in size (Steiner & Gelbloom, 1959), and conglomerate masses forming irregular plaques of variable size over the dura mater were also seen. Histologically, they all showed the typical zonal organisation consisting of palisaded epithelioid cells surrounding a central necrobiotic mass. All patients had multiple subcutaneous and visceral nodules.

Radiological investigation of patients with severe rheumatoid arthritis has been greatly improved by the use of water-soluble, intrathecal contrast medium and computed tomography (CT). Relatively little patient manipulation and table tilting is required to place contrast medium in the cervical subarachnoid space and posterior fossa cisterns, and the potentially hazardous high cervical injection of contrast medium in the presence of disease at the cranio-vertebral junction is usually unnecessary. Lateral radiographs of the cervical region in passive flexion and extension with the patient in a comfortable supine position are usually all that are required for the conventional myelogram; CT

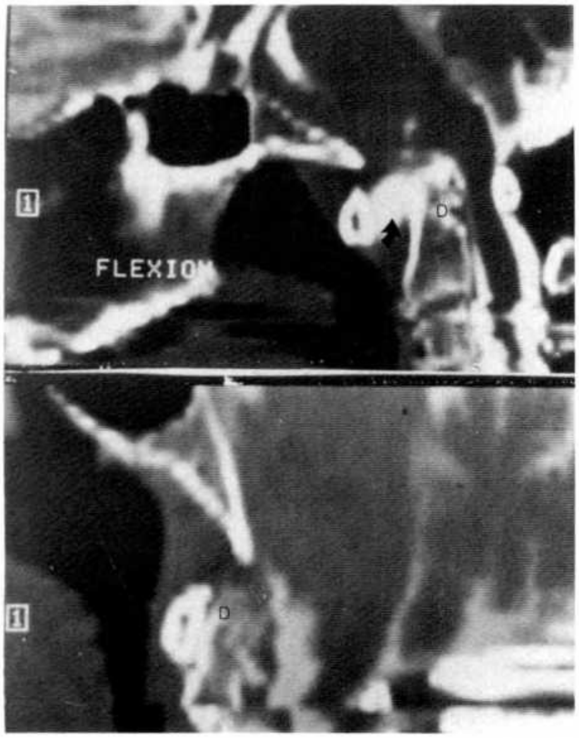

FIG. 3.

Sagittal reformatted images from the myelo-cisternogram. The lower image was made from a set of axial slices with the head extended, although there is considerable misregistration due to patient movement. The dens (D) is eroded and displaced posteriorly to compress the spinal cord only in flexion. The pseudomeningocoele (arrow) is shown in the atlanto-dental interval only on flexion. The mobility of the dens is well shown.

of the cranio-vertebral junction and entire cervical spine may then be performed to obtain more precise information, especially concerning the effects of the bony and soft-tissue abnormalities on the brain stem and spinal cord. The clinical significance of the findings has been the subject of several recent studies reported by our group (Crockard et al, 1985, 1986; Stevens et al, 1986).

Moderate amounts of pannus causing spinal-cord compression at the cranio-vertebral junction have been reported previously (Stevens et al, 1986). However, none has shown such extensive intracranial involvement as this case. Some portions of the mass seemed as though they might have transgressed the dura, though this was not confirmed surgically. It seems probable that the entire mass was pannus because continuity with synovial disease at the foramen magnum was shown, the histology of the specimen obtained at surgery failed to show polarised necrobiotic foci, and the patient had no subcutaneous nodules. Cisternal epidermoid tumours may have a similar appearance on CT. However, the lower part of this mass was biopsied and no epidermoid tissue was found, and the components which were not accessible for biopsy did not seem any different on CT.

A pseudo-meningocoele was the other unusual feature in this case. Meningocoeles are a well known but uncommon feature of the rheumatic diseases, especially ankylosing spondylitis, though usually in combination with widespread dural ectasia (Newton & Potts, 1983). Involvement of the dura by necrobiotic nodules and fibrinoid necrosis is presumed to be the pathological substrate producing weakening and, occasionally, actual perforation of the dura. Focal destruction of the dura and the cruciform and apical ligaments seems the most likely cause of the abnormal cerebrospinal-fluid collection in this case. Its irregular shape suggested that the arachnoid had also been destroyed and that bursae around the dens had come into direct communication with the subarachnoid space. In other words, the collection was more likely to have been a pseudomeningocoele than an arachnoidal diverticulum. This being so, it was surprising that the surgeon did not unavoidably encounter cerebrospinal fluid during the odontoidectomy. Presumably, thick granulation tissue had effectively obliterated most of the anterior dental bursa, though the general destruction of soft tissues in the region allowed the meningocoele to penetrate into the void created by the wide atlanto-dental interval in flexion. On extension this void was obliterated and the slit-like atlanto-dental interval must have been occupied only by granulations, not by the compressed meningocoele.

Transoral odontoidectomy combined with occipito-atlanto-axial fusion as a one-stage procedure so far seems to offer the best chance of remission and the lowest morbidity for patients with myelopathy associated with rheumatoid disease affecting the cranio-vertebral junction (Crockard et al, 1985; Stevens et al, 1986). This being so, one would expect the operation to be performed with increasing frequency in the future. The vertebral artery has sometimes been encountered near the midline behind the anterior arch of the atlas in cases with marked atlanto-axial rotation, and this case suggests that the subarachnoid space also may be encountered in this situation. Anticipation of this possibility pre-operatively here was helpful to the surgeon in preventing a cerebrospinal-fluid fistula. The value of obtaining images with the neck in flexion and extension at myelography was also emphasised.

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Wandering spleen

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Ectopic or wandering spleen is a rare anomaly. We report on a case discovered as an incidental finding during intravenous digital subtraction angiography (DSA) of the renal arteries.

CASE REPORT

A 65-year-old lady with resistant hypertension was referred for intravenous DSA to exclude renal artery stenosis. No stenosis was demonstrated but it was noted that the splenic artery, though arising from its normal site, passed caudally to supply a spleen which lay entirely below the left kidney at the pelvic brim. No other splenic tissue was seen (Fig. 1). To confirm these unusual findings, ultrasound and isotope liver scans were performed. The aberrant location of the spleen was confirmed by ultrasound. However, $^{99}Tc^{m}$ sulphur colloid liver scans showed the spleen to be conventionally located while the patient was examined in the usual supine position. When the patient stood, however, the spleen was seen to move down into the region of the pelvic brim (Fig. 2). It therefore appeared that the patient's spleen was excessively mobile and sometimes assumed an ectopic location.

DISCUSSION

An aberrant location of the spleen is a rare occurrence. In various reviews of splenectomies the incidence has been reported as two out of 1003 (Pugh, 1946), four out of 1413 (Eraklis & Filler, 1972) and none out of 1437 (Whipple, 1939). The increased mobility of the spleen is due to lengthening and/or laxity of its suspensory ligaments. Abell (1933) found that the pedicle was up to 10 in long in such cases. The cause of this increased lengthening or laxity may be congenital, arising as a result of incomplete fusion of the dorsal mesogastrium. Evidence for this is that the tail of the pancreas is sometimes included in the intraperitoneal splenic hilum (Abell, 1933; Michaels, 1954; Woodward, 1967; Carswell, 1974; Smulewicz & Clemett, 1975). Some cases have also been noted to have a persistent mesentery of the descending colon (Carswell, 1974). There is also an increased incidence in females. Only five of Abell's series of 97 patients were male (Abell, 1933). The incidence is also further increased in multiparous women, suggesting a possible hormonal cause. Abdominal wall laxity and splenomegaly have also been suggested as causative factors (Abell, 1933; Gordon et al, 1977).

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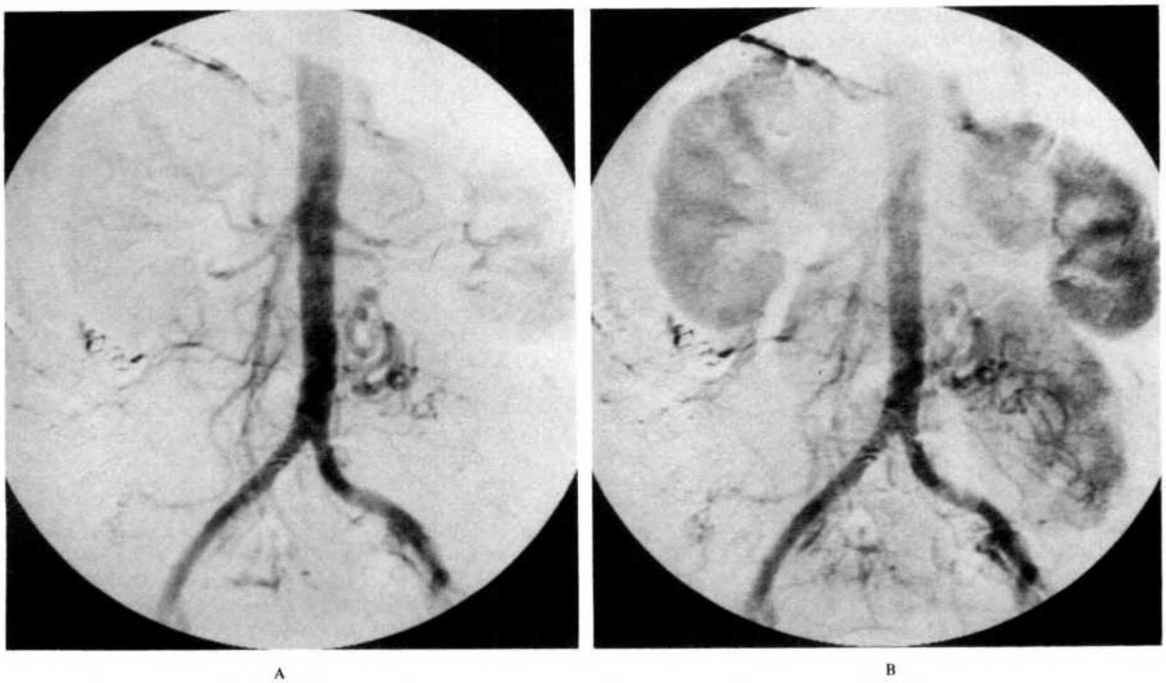

FIG. 1.

Two DSA images of the abdomen. The image in (A) shows the typically coiled splenic artery arising in a normal position but then passing caudal to the left renal artery. The image in (B) shows the splenogram lying beneath the left nephrogram.

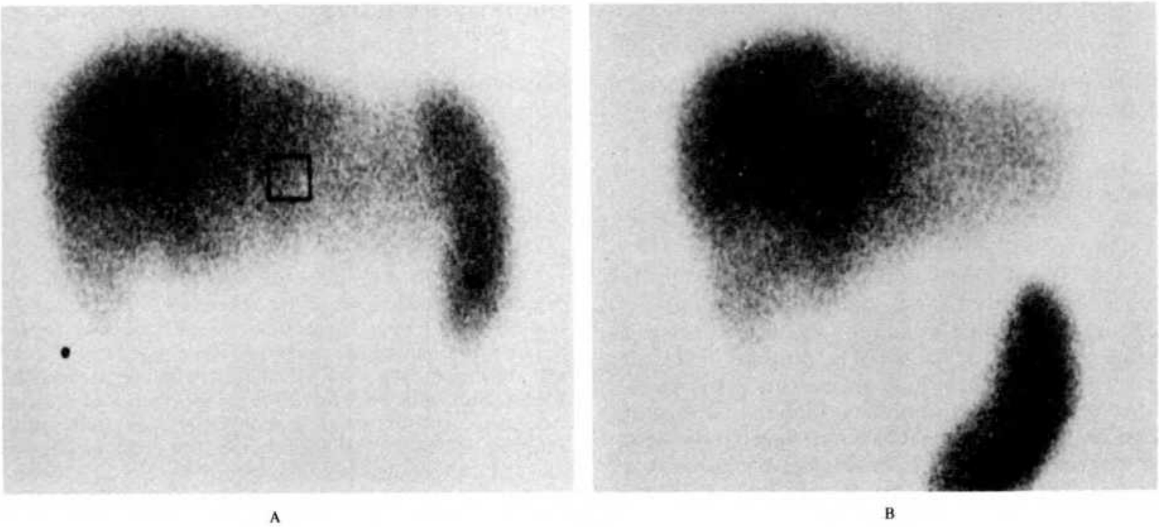

FIG. 2.

Two images from a $^{99}Tc^m$ sulphur colloid liver scan. The image in (A) is taken with the patient supine and shows the spleen as apparently lying in a normal position. The rectangle represents the xiphisternum and the two laterally placed dots represent the inferior costal margins. The image in (B) is taken with the patient erect and shows the spleen now lying much lower.

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Patients may present with an abdominal mass, colic or pelvic discomfort or acute torsion. All of Abell's 97 patients ultimately presented with acute torsion. According to recent authors, the mortality associated with splenic torsion is 50% (Gordon et al, 1977; Abrams, 1983). However, the reference they quote in support of this figure is Abell's paper (1933), which actually quotes an overall mortality of 17 6%, rising to 42 5% in pregnancy and the puerperium. Furthermore, these cases were all documented from 1885 to 1933 and one would expect that current medical practice would reduce these figures significantly. Indeed, the later, though smaller, series report 100% survival (Simpson & Ashby, 1965; Woodward, 1967; Carswell, 1974; Smulewicz & Clemett, 1975; Gordon et al, 1977). Current clinical practice is to observe these patients and to perform splenectomy or occasionally splenopexy should they develop an acute abdomen.

Our patient has remained well but she and her medical practitioner are now aware that, should she develop an acute abdomen, then the diagnosis of splenic torsion must be considered.

Our case illustrates the following two practical imaging points. (1) During intravenous DSA procedures it is important to visualise the whole of the abdominal aorta and not to look exclusively at the presupposed area of interest. Otherwise, potentially important abnormalities may be missed. (2) In isotope scanning, a normally located spleen with the patient in a supine position does not exclude a wandering spleen.

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The detection of massive colonic haemorrhage by selective coeliac arteriography

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The usual blood supply to the large intestine (Fig. 1) is adequately described in standard anatomy books, but many do not mention a clinically significant anatomical variation, the arc of Riolan. The purpose of this case report is to document this arterial anomaly, since it played an important role in the arteriographic diagnosis of massive gastrointestinal haemorrhage. To the best of our knowledge, this is the first reported case where a selective coeliac arteriogram demonstrated a bleeding colonic lesion.

Case Report

A 71-year-old man was seen as an emergency because of massive rectal bleeding. He had no significant past history or family history. The blood pressure on admission was 140/80 mm Hg and his pulse was 90/min Rectal examination revealed dark, red blood on the examining finger. Except for blood in the lumen, sigmoidoscopy and colonoscopy were negative up to 35 cm. Endoscopy of the oesophagus, stomach and duodenum was unremarkable. The initial haemoglobin level was 13.3 g/dl, but dropped to 9 4 g/dl within a few hours An emergency coeliac arteriogram (Figs 2, 3) demonstrated extravasation of contrast agent in the right upper quadrant of the abdomen, which was interpreted as bleeding from a duodenal diverticulum Because of persistent bleeding per rectum and a drop in the systolic pressure to 90 mm Hg, no further arteriographic study was carried out. Immediate laparotomy was performed and the colon was seen to be filled with blood A gastrostomy and four enterostomies showed no evidence of blood in either the stomach or small intestine A colonoscope was passed per rectum through the colon, and

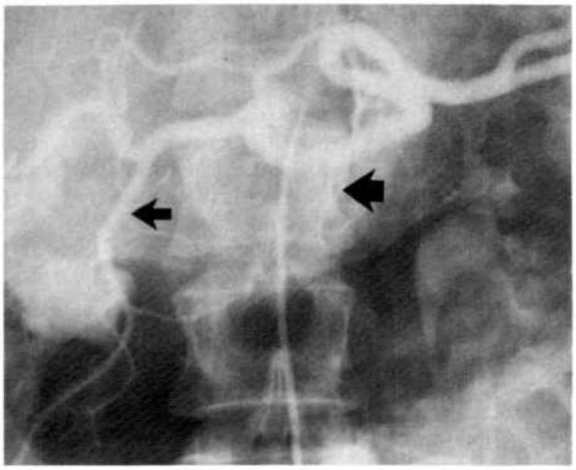

FIG. 1.

Normal coeliac arteriogram showing the gastroduodenal artery (small arrow) and small dorsal pancreatic branches (large arrow).

when the tip reached the caecum, the lumen was seen to be filled with blood.

The surgeon's diagnosis was of a bleeding site in the caecum, probably an arterio-venous malformation, and a right hemicolectomy was performed. The patient had an uneventful post-operative course. The pathologist examined the terminal ileum, caecum and right colon specimen but could not find the site of bleeding. An incidental finding was lymphoid hyperplasia of the terminal ileum.

DISCUSSION

The unique feature of this case was the demonstration of a colonic bleeding site by selective coeliac arteriography. The operative findings necessitated a review of the coeliac arteriogram, and this disclosed the presence of an arc of Riolan, which supplies coeliac blood to the hepatic flexure of the colon.

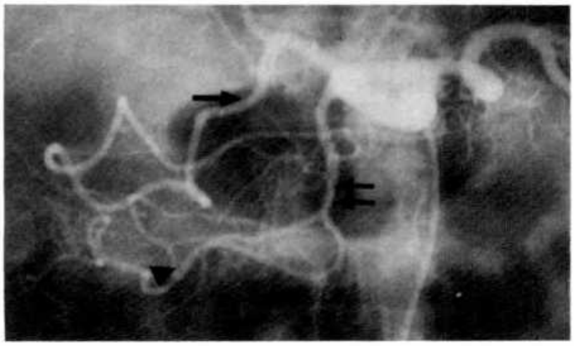

FIG. 2.

Early arterial phase of a selective coeliac arteriogram of the patient. The gastroduodenal artery (arrow), arc of Riolan (double arrow) and accessory middle colic branch to hepatic flexure (arrowhead) are shown.

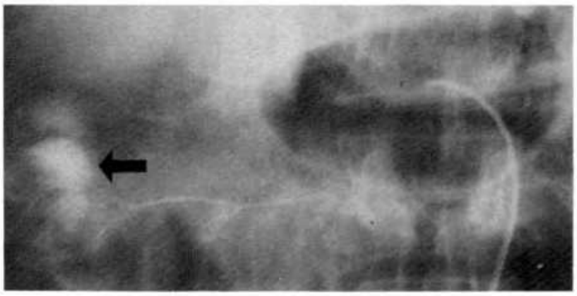

FIG. 3.

Late venous phase of the selective coeliac arteriogram, showing contrast agent within the lumen of the hepatic flexure (arrow).

In order to understand this arterial variant, it would be appropriate to recapitulate the basic arterial anatomy of the subdiaphragmatic gastrointestinal tract. As a rule, the coeliac artery, via its three branches, is the exclusive source of blood to the stomach. The coeliac artery also supplies most of the blood to the proximal portion of the duodenum, the remainder being delivered by the inferior pancreaticoduodenal branch of the superior mesenteric artery. The superior mesenteric artery is the only source of blood to the remaining portion of the small intestine. It also irrigates the caecum, ascending colon and the proximal two-thirds of the transverse colon. The remaining portion of the colon, as well as the rectum, is supplied by the inferior mesenteric artery.

Anatomical variations in the blood supply to the gastrointestinal tract are common and there are said to be 3000 variations in the supply to the abdominal organs (Michels, 1955). While many of these are of interest only to the professional anatomist, variations in the blood supply to the biliary duct system and the liver are important to the surgeon. For example, some of the hepatic branches of the common hepatic artery may be congenitally absent, and the blood supply to a portion of the liver will then arise from branches of the superior mesenteric artery. This variant is also important for intra-arterial chemotherapy of the liver.

Many anatomy books indicate that the right colic artery is a separate branch of the superior mesenteric artery, but arteriographic examinations and anatomical dissections indicate that this is true in only 34% of cases. In 57% of the population, the right colic and middle colic arteries arise as a common trunk to supply the caecum, ascending colon and the proximal two-thirds of the transverse colon. This type of information may be vital to a surgeon replacing the oesophagus with a segment of the colon.

The anatomical variation discovered in our patient consisted of a blood supply to the hepatic flexure of the colon from a branch of the coeliac artery. More specifically, the dorsal pancreatic branch of the splenic artery continued caudally to form an accessory middle colic artery supplying the hepatic flexure of the colon. Hence, a selective injection into the coeliac artery visualised the bleeding lesion in the hepatic flexure of the colon and not, as was thought, in the duodenum.

This arterial anomaly has been described by several authors, either from anatomical dissections (Michels, 1955) or from arteriography (Moskowitz et al, 1964; Nebesar et al, 1969). On the basis of hundreds of dissections, Michels found that 14% of the population will have a middle colic artery arising as a branch of either the dorsal pancreatic or the transverse pancreatic arteries. This anatomical variation is called the arc of Riolan. The dorsal pancreatic artery itself is highly variable. In 39% of the population it arises from the first part of the splenic artery, but in 22% it arises directly from the coeliac artery (Michels, 1955).

A review of the embryology and comparative anatomy helps in understanding why there are so many anatomical variations in the blood supply to the intra-abdominal gastrointestinal tract. When the arterial system is first developed, there are two dorsal aortas. In the thorax and abdomen these two dorsal aortas later fuse into one aorta. In the 7 mm embryo, the coeliac artery is seen to arise from the aorta at the level of the fourth thoracic segment. By the time the embryo is 17 mm long, however, the coeliac artery has migrated to the level of the 12th thoracic vertebra by making new rootlet connections with the aorta along the way. A similar caudal migration of the superior mesenteric artery also occurs. In the early embryo, vascular bridges are present between the coeliac artery and the superior mesenteric artery (Tandler, 1903, 1904). Most of these vascular connections normally become atretic, but anomalies occur when they persist.

In the higher vertebrates (man, dog, cat) the coeliac and superior mesenteric arteries are separate vessels. The close embryological association of these arteries is illustrated, however, by the fact that they are normally fused in the adult frog, salamander, spiny anteater, duck-billed platypus and mole.

In this patient, neither the surgeon nor the pathologist were able to detect a cause of this massive haemorrhage It is the authors' contention that the bleeding probably arose in a diverticulum of the hepatic flexure. It is well known that right-sided colonic diverticula are the most common cause of massive lower intestinal haemorrhage in the elderly. In retrospect, selective coeliac arteriography clearly showed extravasation of contrast agent in the region of the hepatic flexure, a segment supplied by the arc of Riolan. On external examination of the colon by the surgeon, however, the diverticulum may be hidden by mesenteric fat. Although the arteriogram localised the site of the bleeding, Brandt (1984) found that in only eight out of 43 patients was he able to prove by arteriography that the aetiology was a diverticulum.

The next most common cause of massive lower intestinal haemorrhage in the elderly is angiodysplasia of the colonic mucosa. These are found predominantly in the caecum and ascending colon. On selective visceral arteriography, angiodysplasia can be diagnosed from the presence of a cluster of arterioles and by early and persistent filling of dilated, tortuous veins at the site of the lesion. These cardinal features were absent in our patient, and we therefore doubt that angiodysplasia was present. With standard histological techniques even the pathologist will frequently not be able to make the diagnosis of angiodysplasia and several authors have utilised intra-arterial injection of the specimen with a silicone-rubber compound to demonstrate submucosal, ectatic and tortuous veins better (Brandt, 1984).

Other, less common causes of massive haemorrhage per rectum include peptic ulcer, small intestinal diverticula, neoplasm, colitis, varices, tuberculosis, Crohn's disease, splanchnic artery aneurysms and aorto-enteric fistulas.

It is of interest to note that, since the introduction of selective visceral arteriography, the number of unlocalised cases of gastrointestinal bleeding has decreased from 26.6% to 3.1% (Mitty et al, 1969).

In conclusion, a case has been presented where knowledge of an unusual arterial anomaly (the arc of Riolan) was essential to the understanding of how a coeliac arteriogram could demonstrate massive bleeding in the hepatic flexure.

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Case reports

Unilateral juvenile hypertrophy of the breast

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Juvenile hypertrophy (also called adolescent hypertrophy) of the breast is a well known occurrence, the aetiology of which is uncertain (Mayl et al, 1974; Wise, 1976). Occasionally, it is unilateral and mammography is needed to exclude an underlying tumour. We report a case that presented mammographically as a discrete mass with calcifications suggestive of a fibroadenoma No report of similar cases could be found in the literature

CASE REPORT

A 19-year-old woman noted normal enlargement of both breasts during her first pregnancy After delivery, the right breast returned to its previous size but the left breast decreased only slightly. In a second pregnancy, the left breast had markedly enlarged necessitating admission to hospital with a presumptive diagnosis of cystosarcoma phylloides. Mammography at that time revealed no discrete masses An open biopsy was interpreted as "cystic dilatation of ducts and acini with secretory changes". No further treatment or investigation was done.

At 28 years of age the patient presented to our clinic in her third pregnancy with further enlargement of the left breast which had continued slowly since the second pregnancy, with a marked acceleration of growth in the last 4 months. Radiological examination included ultrasound which showed numerous dilated blood vessels The breast tissue was solid with no cystic areas but there were several areas of intense shadowing consistent with calcifications. Low-dose film mammography showed a discrete mass which measured 17 cm × 18.5 cm in the left breast (Fig 1) with a halo effect seen around some parts of the mass margins. Dense, coarse calcifications were present in the centre of the mass. This was interpreted as a giant fibroadenoma, with cystosarcoma phylloides as a second possibility The patient underwent a spontaneous abortion and requested a reduction mammoplasty. The left breast was massively enlarged, 10 to 15 times the size of the right breast Dilated superficial veins and superficial ulcerations were present in the outer quadrants (Fig. 2) Several large, ill-defined masses throughout the breast were consistent with fibrous change. At surgery, 1220 g of very floppy, delicately encapsulated fibro-fatty tissue was removed and a subpectoral silicone implant inserted. Histologically, the tissue contained multiple areas of calcification and was noted to be very nodular The pathological diagnosis was juvenile hypertrophy with focal calcification.

DISCUSSION

Some asymmetry of the breasts is normal, with the left breast usually the larger Several conditions may cause asymmetry, including abnormal development, tumours, surgery, radiation therapy, and trauma. Of these, developmental anomalies account for the majority (Berakla, 1978). Juvenile hypertrophy of the breast typically occurs during adolescence following a normal puberty. Instead of normal development ceasing after a certain point, the breast continues to grow even into mature years. This is usually bilateral, but may affect one breast more than the other (Haagensen, 1971). There have been a few reported cases of massive breast hypertrophy during pregnancy (Williams, 1957) in which enlargement begins soon after conception, usually during the second pregnancy. In our patient, onset occurred during the first pregnancy with some regression after delivery. Enlargement continued during and after her second pregnancy, accelerating in the third pregnancy.

Histological examination of juvenile hypertrophy shows little that can be termed abnormal. The epithelial elements are unremarkable and the excessive growth appears to involve the connective tissue and fat. No mention is found in the literature of calcification being associated with these lesions either mammographically or pathologically. It is interesting that the mechanism of calcium formation in fibroadenomas is not clear, but it is thought to be via central necrosis, saponification and, finally, calcium deposition (Martin, 1982). The calcifications in fibroadenomas can be of several types, and may or may not be associated with a mass. If large and within a mass or peripheral to it, they are easily recognised as typical of a fibroadenoma. The large, dense, bizarre-shaped calcifications, seen in this case, are representative of myxoid degeneration and are commonly seen in fibroadenomas. Small, irregular calcifications are suspicious of malignancy (Wolfe, 1977). In a lesion as large as the one in our patient, myxoid degeneration would seem very likely. This would explain why the calcifications seen mammographically had the same appearance as those commonly seen in fibroadenomas. We found no reference in the literature to cases of juvenile hypertrophy presenting mammographically as discrete masses but Furnas (1982) reports a case of bilateral hypertrophy, with the tissue found to be a single discrete mass at surgery. The mammographic picture in this patient was of giant fibroadenoma. It should be kept in mind, therefore, that juvenile hypertrophy can present with an identical appearance.

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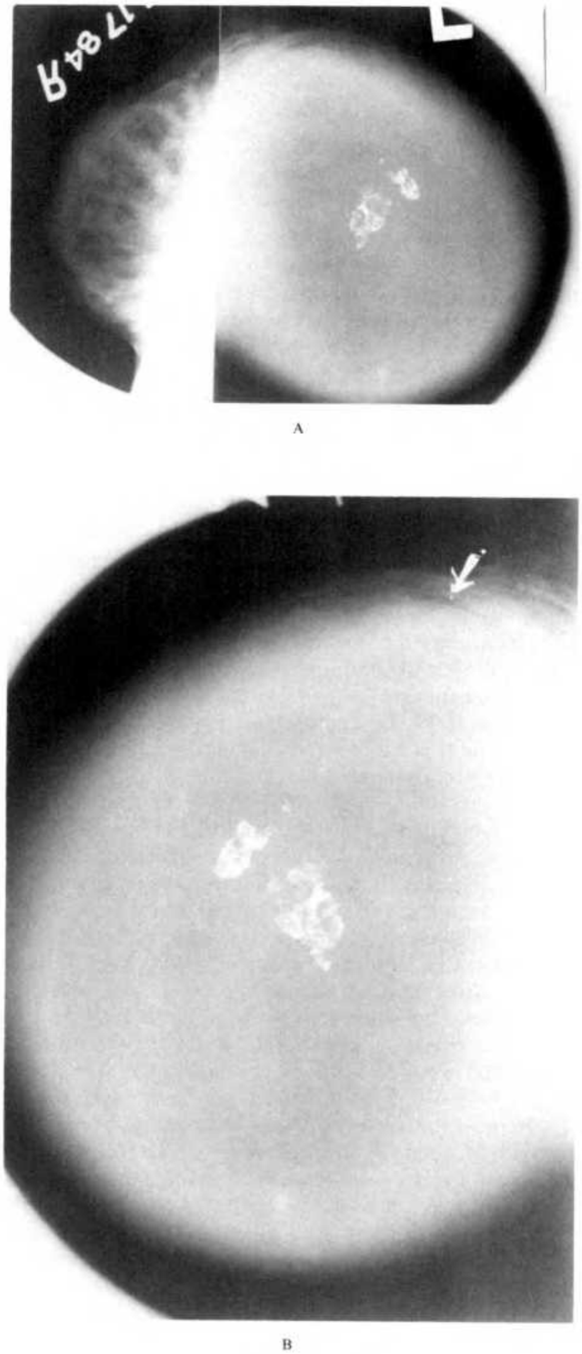
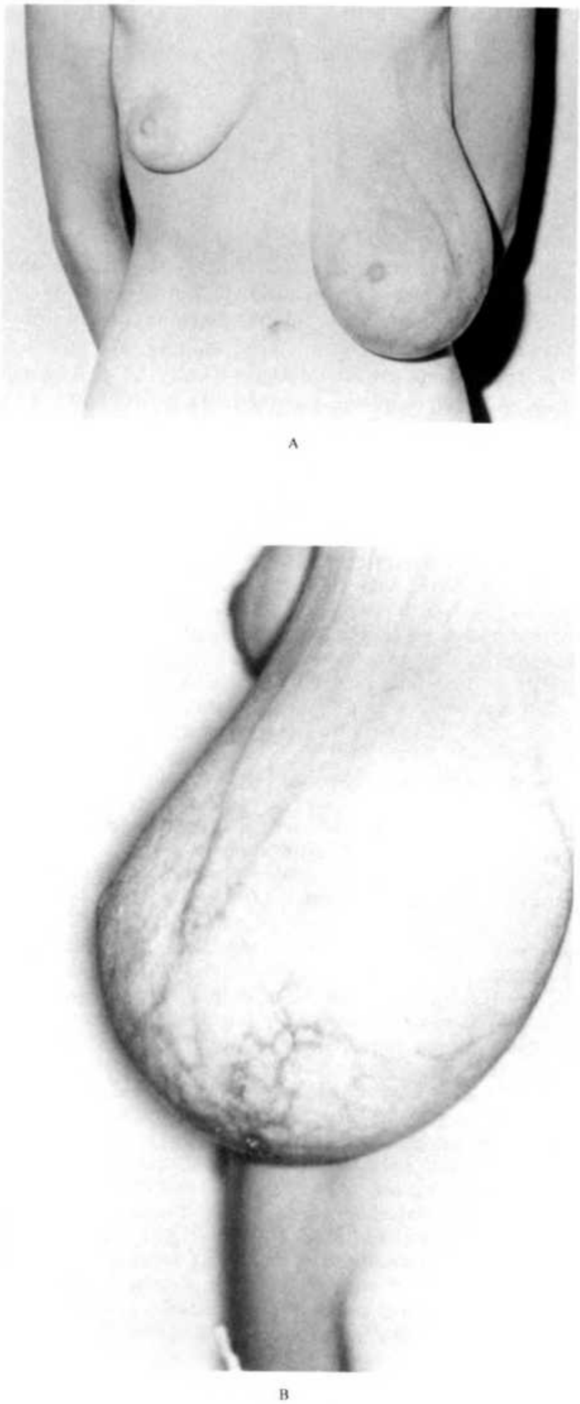


A

B

FIG. 1.

Low-dose mammography. (A) Contact lateral view of both breasts. Normal right breast; mass in left breast. (B) Closer view of mass on left with coarse calcifications. Halo-effect (arrow) is seen superiorly.



A

B

FIG. 2.

The patient's physical appearance. (A) Frontal view and (B) lateral view of left breast.

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Anuria: an unusual presentation of aortic dissection (diagnosed by ultrasound)

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Presentation of dissecting aneurysm as a renal problem is rare. Demos et al (1981) describe three cases and found only four others in the literature (Hirst et al, 1958; Mulder & Kaufman, 1968). This case is exceptionally unusual in that the final presentation was of oliguria: pain, at the last admission, was not a feature.

The diagnosis of dissection could be made on abdominal real-time two-dimensional ultrasound and Doppler ultrasound and was confirmed by aortography.

CASE REPORT

A 71-year-old man was admitted complaining of failure to pass urine for 24 h. He had undergone right nephrectomy for tuberculosis 20 years previously and, more recently, had been admitted 2 months earlier with chest pain radiating into his back and abdomen. This pain was considered myocardial in origin, although there were no electrocardiographic or enzyme changes to confirm infarction. At that time, he was found to be hypertensive (220/120 mm Hg) and was treated with beta-blockade and diuretics.

On the current admission, he was noted to be generally unwell, but well hydrated and normotensive with no signs of anaemia, jaundice or cyanosis. On examination, his pulse was regular and the blood pressure 140/95 mm Hg. All peripheral pulses were present and no abnormal physical signs were detected on auscultation. The aorta was prominent and pulsatile in the epigastrium and a nephrectomy scar was seen over his right loin. The left kidney and bladder were not palpable. Rectal examination revealed his prostate to be normal in size and consistency and catheterisation of the bladder failed to obtain any urine.

Real-time ultrasound demonstrated a normal left kidney, without evidence of pelvicalyceal or ureteric distension. However, before further investigations were pursued, the patient began to pass urine, subsequently producing 2 l in 24 h, before relapsing into anuria.

In view of the previously noted pulsatile abdominal aorta, repeat ultrasound examination was made of the aorta and kidney. Real-time ultrasound examination of the aorta demonstrated a single, intraluminal echogenic septum consistent with an intimal flap (Figs 1, 2) which extended throughout the entire abdominal aorta, from the diaphragm to its bifurcation. Use of Doppler ultrasound with two-dimensional real-time imaging confirmed flow in the true lumen on one side of the flap and absence of significant flow on the other side, in the false lumen. The left renal artery was identified arising from the aorta and no significant flow detected within it. No aortic valvular regurgitation was detected in the left ventricular outflow tract by Doppler ultrasound from a cardiac apical "window". An aortogram

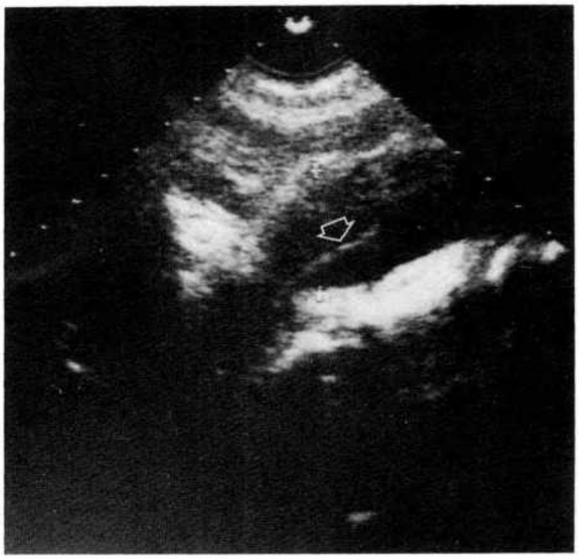

FIG. 1.

Abdominal aorta, longitudinal scan. The intimal flap is shown.

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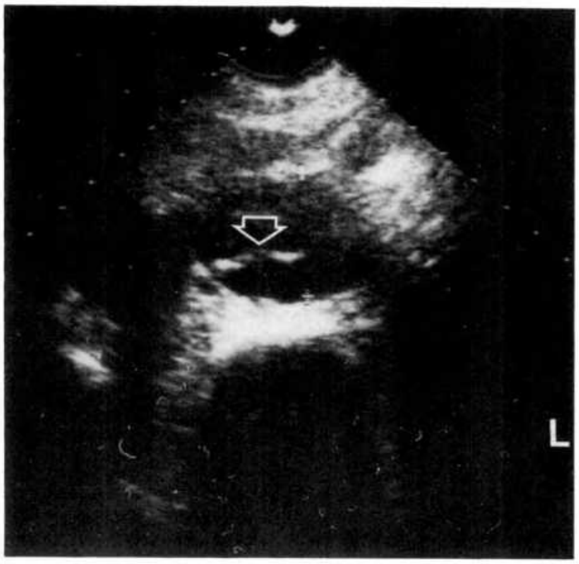

FIG. 2.
Transverse scan of abdominal aorta, showing intimal flap.

was performed from the right femoral artery which confirmed an extensive aortic dissection arising in the aortic arch, just distal to the origin of the left subclavian artery extending to the bifurcation of the aorta, spiralling round the abdominal aorta and extending into the origin of the left renal artery, De Bakey Type III (De Bakey et al, 1965). In contradistinction to the Doppler findings, the true lumen of the distal abdominal aorta was completely obliterated, with the iliac vessels filling late by collaterals, and the lumen of the left renal artery was involved in the dissection. While the intrarenal arteries were opacified during the pressure injection, there was no subsequent nephrogram nor pyelogram (Figs 3, 4).

In view of the extent of the dissection, it was felt that surgical repair was unlikely to be successful.

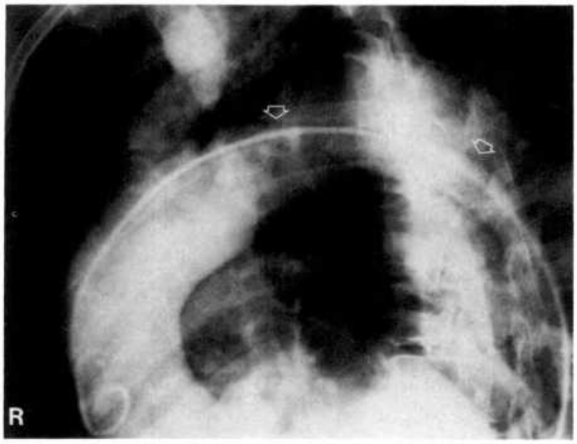

FIG. 3.
Arch aortogram; intimal flap (arrowed) arising distal to the left subclavian origin.

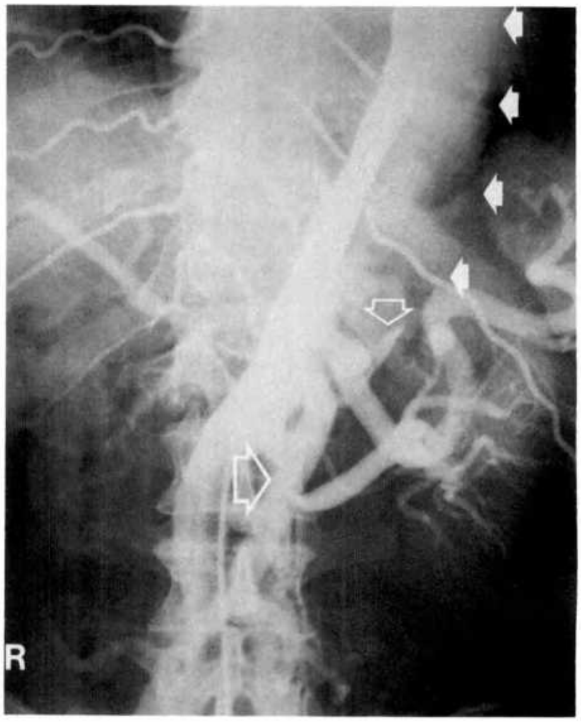

FIG. 4.
Lumbar aortogram; dissection involving proximal part of left renal artery (horizontal solid arrows), some backflow of contrast medium (vertical arrow) into false lumen (horizontal open arrow).

Following the investigations, the patient's urine output returned again for a few days. However, he subsequently became permanently anuric and died, after 10 days, in renal failure.

In retrospect, it was felt that the dissection had begun at least as early as the admission with chest pain, 2 months previously.

DISCUSSION

Demos et al (1981) noted that aortic dissection presenting primarily as a renal tract problem is rare. This case is unusual in that intermittent complete anuria was found to be due to extensive aortic dissection involving the origin of the renal artery to a solitary kidney.

The left renal artery is more commonly involved in dissection than the right (Siegelman et al, 1970). Diminished or absent nephrogram or a nephrogram without the subsequent appearances of contrast medium within the calyces suggests that the kidney is severely ischaemic.

In this case, the intrarenal arteries opacified, possibly as a result of the pressure supplied by the pump injection, but there was no subsequent nephrogram nor pyelogram, indicating severe renal ischaemia.

We were able to make the diagnosis during ultrasonic examination of the aorta. Similar identification of abdominal dissection was described by Bresnihan and Keates (1980) by B-scanning. With Doppler imaging now available, both the cause and the effect of the renal artery involvement by dissection can be shown. We postulate that the intermittent episodes of anuria were caused by some form of intimal flap effect, either in the renal artery itself, at its origin, or even more proximally, which temporarily reduced renal artery perfusion to a level which precluded filtration.

We would like to stress that aortic dissection should be considered and sought ultrasonically in patients with anuria, even in the absence of pain at the time of presentation, particularly if the patient has only one kidney.

ACKNOWLEDGMENTS

We would like to thank Dr C. Johnson and Dr J. B Penry for their help in the preparation of this report, and also Dr P Harrison for his permission to report on his patient

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Book reviews

Essentials of Orthopaedic Surgery By Alfred T. Williams, pp. 236, 1986 (Churchill Livingstone, Edinburgh; Pitman Publishing Ltd, London), £12.95.
ISBN 0-272-79828-2

This volume is, as its title suggests, an introduction to the practice of orthopaedic surgery. The book will doubtless find a place on the bookshelves of students and junior doctors dealing with trauma. The layout is concise, clear, and accompanied by many line drawings which have an instant impact and will be readily understood by anyone reading the volume. The emphasis is on bone trauma and the mechanics of fracture and the theory and practical application of reduction forces in healing are dealt with from fundamental principles. The sections on tumours and bone infection are rather brief, clearly indicating that the purpose is the teaching of practical management rather than diagnosis.

Arthritic conditions are, again, dealt with rather as mechanical problems, which is indeed what they are to the orthopaedic surgeon, and the surgical correction of deformities and joint replacement is clearly discussed, the line drawings simplifying the presentation.

The author obviously regards diagnosis as beyond the brief of his volume and the absence of radiographs will render the book of rather limited value to the radiologist. However, the trainee will find useful information in its pages and the more senior radiologist will find the straightforward approach of use when studying the mechanics of bone and joint injuries.

Mr Williams has presented a very complex and difficult subject in a straightforward way and the book will have appeal to anyone concerned with orthopaedic treatment.

N. H. CROSBY

Cervico-Occipital Joint (RX, CT). By A. Wackenheim, pp. ix + 192, 1985 (Springer-Verlag, Berlin), DM35.
ISBN 3-540-15327-6

At first sight this is an unimposing looking little book, opening with a quotation from Oscar Wilde: "The true mystery of the world is the visible, not the invisible". The quotation is particularly apt, for much of the language in the text is indeed mysterious. The author, confessedly, is concerned principally with the philosophical aspects of analysing visual data and has developed a system adapted from structuralism and phenomenology. However, many technical terms such as "signifiant" and "signifie" and some common words used in an unusually precise and restricted sense I did not find adequately explained in the introduction. Moreover, even in those sections devoted to narrative, the text lacks lucidity, partly because it derives from an over-literal translation and also because its language is intentionally laconic.

Professor Wackenheim is a prominent personality in European radiology and the subject is one on which he has published extensively. The quality of the material and its interpretation is easily palpable. His aim throughout is didactic, and the general layout, I felt, achieved the intention of making its lessons memorable. Over 90% of the material consists of plain radiographs and conventional tomograms and less than 10% computed tomography, and it is limited almost entirely to a selection of skeletal abnormalities.

This is intentionally not an easy book to read. After a few pages I found myself wondering whether it was worth the effort, and in the end my answer was a guarded "yes". There is probably a place for this type of analysis of visual data, although I am confessedly not converted into a commitment by this demonstration.

J. M. STEVENS

1987, *The British Journal of Radiology*, *60*, 199–200 FEBRUARY 1987

Case of the month

Did he fall or was he pushed?

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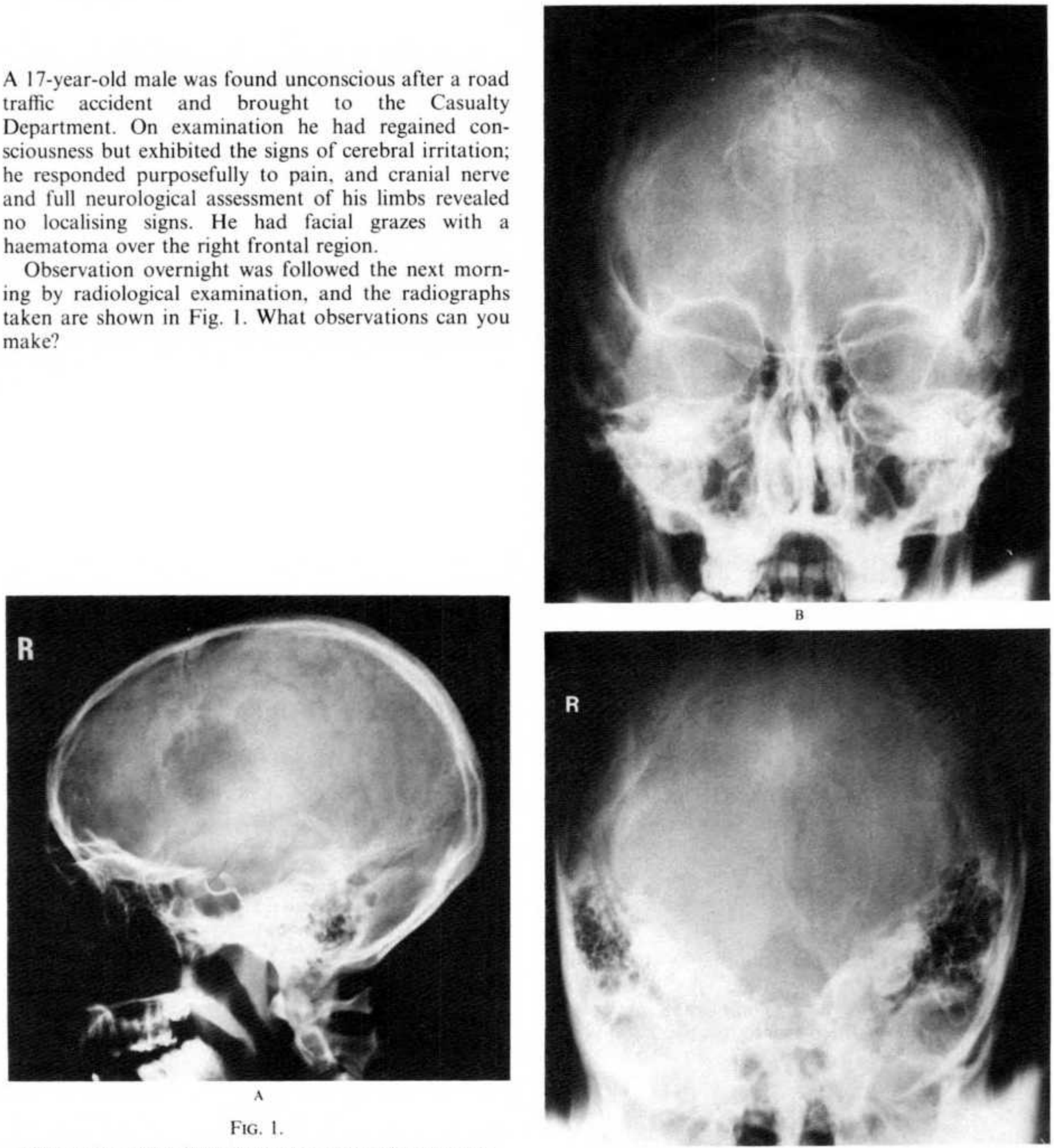
(*Received May 1986*)

A 17-year-old male was found unconscious after a road traffic accident and brought to the Casualty Department. On examination he had regained consciousness but exhibited the signs of cerebral irritation; he responded purposefully to pain, and cranial nerve and full neurological assessment of his limbs revealed no localising signs. He had facial grazes with a haematoma over the right frontal region.

Observation overnight was followed the next morning by radiological examination, and the radiographs taken are shown in Fig. 1. What observations can you make?



B

A

C

FIG. 1.

Radiographs of the skull taken on morning after accident.

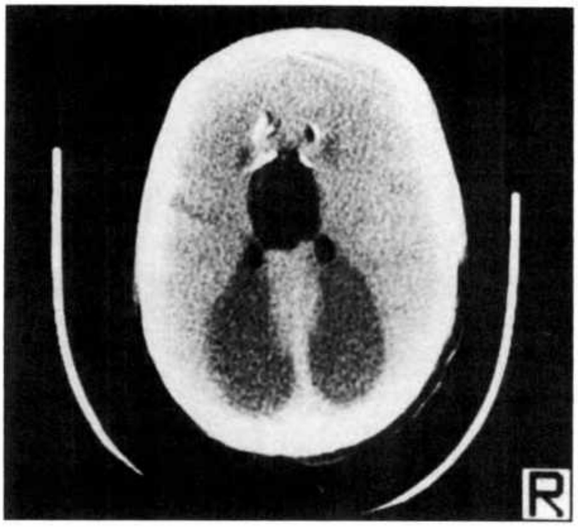


FIG. 2.

A CT scan (L+20, W 75), showing central, fat-attenuation mass with calcification in its capsule, associated with symmetrical dilatation of the posterior horns of the lateral ventricles.

Two linear parietal fractures are shown. In addition, however, there are several areas of abnormal calcification; curvilinear in shape, they are present one on each side of the midline and their full extent is best shown on the Towne's projection. The lateral radiograph also shows an area of unusually low density within the line of calcification.

These features are typical of a lipoma of the corpus callosum; computed tomography confirmed its nature and site (Fig. 2) and, in addition, revealed ventricular dilatation.

Clinical progress

The patient recovered satisfactorily from his head injury and suffered no subsequent problems. He was referred, however, to the Neurosurgical Department where it was decided to follow him up as an outpatient.

It was decided not to intervene surgically, at least initially, but the possibility of a future shunting procedure to relieve his hydrocephalus was considered likely to become necessary.

No drug therapy was prescribed.

DISCUSSION

A lipoma of the corpus callosum is an unusual, benign tumour of the central nervous system, and produces characteristic features on plain radiographs of the skull because of the presence of calcium within its capsule. It occurs in the region of the genu of the corpus callosum, though on occasion it may extend downward into the septum.

Such a tumour produces symptoms in approximately 50% of cases, these varying from fits and hemiplegia to minor disturbances such as headaches, vertigo, vomiting unrelated to raised intracranial pressure, or emotional lability (Wallace, 1976). They are considered to be congenital and about half of the reported cases are associated with agenesis of the corpus callosum itself. In some of these cases, associations have also been recognised with midline dysraphic defects such as hypertelorism, median cleft nose, myelomeningocoele, agenesis of the cerebellar vermis, or spina bifida.

Six cases have been reported in which a lipoma of the corpus callosum has been associated with a defect in the frontal bone (Kushnet & Goldman, 1978). Lipomas of the corpus callosum may cause hydrocephalus, as was the case in our patient as shown by dilatation of the posterior parts of the lateral ventricles on the CT scan.

Computed tomography clearly defines the lesion and, by assigning it a negative attenuation coefficient, is the most effective and least invasive tool in establishing the diagnosis of a lipoma of the corpus callosum (Harwood-Nash, 1977).

If angiography is performed, then displacement of the pericallosal arteries is seen to be present; the arteries are either incorporated within or lying on the surface of the tumour (Wolpert et al, 1972).

Although relief of hydrocephalus may be indicated if severe, treatment is usually conservative; indeed, surgery carries a high mortality due to involvement of the anterior cerebral arteries in the tumour, and to its great intrinsic vascularity.

Very few instances of uneventful recovery from surgery have been reported in the literature and in only one case was the patient's condition improved by complete removal.

Anti-convulsants may be indicated if the patient suffers epileptic fits; interestingly, the fits do not seem to be related to local pressure as there is no sign of pressure atrophy on the adjacent brain tissue.

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1987, *The British Journal of Radiology*, 60, 201–203 FEBRUARY 1987

Short communications

Iodinated contrast agents as "radiosensitisers"

By P. Dawson, *Miranda Penhaligon, *Eileen Smith and †J. Saunders

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The sole purpose of radio-contrast agents is to increase the absorption of X rays in blood vessels and soft tissues. Current diagnostic agents take advantage of the properties of iodine with its acceptably low clinical toxicity and moderately high atomic number (53), the latter yielding a relatively large absorption coefficient for photons in the diagnostic X-ray energy range, owing to the photoelectric effect. One consequence of this, not often appreciated, is that cells in the vicinity of an iodine-rich solution will receive a higher radiation dose than would be the case if iodine were not present. This is partly responsible for the reported cytogenetic changes in lymphocytes *in vitro* and *in vivo* (Adams et al, 1977; Norman et al, 1978; Cochran et al, 1980; Cochran & Norman, 1982; Hadaghy et al, 1982). Though these data clearly signal an undesirable, if unavoidable, phenomenon in diagnostic radiology, such a cytotoxic effect may be capable of exploitation in radiotherapy.

To examine this latter possibility, cells *in vitro* were treated with various concentrations of the contrast agent meglumine ioglycamide (Biligram, Schering AG) and subjected to orthovoltage X rays. Marked radiation enhancement was obtained at an iodine concentration of 50 mg ml^{-1}, a concentration that is well within the range achievable in the bloodstream.

METHOD

Chinese hamster ovary (CHO) cells were grown in monolayer culture in Hepes-buffered minimum essential medium (MEM) supplemented with 15% fetal calf serum, non-essential amino acids and L-glutamine. Tissue culture flasks (25 cm^2; Nunclon) were seeded with 3.5×10^5 cells 24 h before irradiation, so that cells were in the exponential phase of growth during treatment.

Biligram was obtained as a 17% aqueous solution (85 mg ml^{-1} iodine) and diluted with complete medium to the required concentration. Biligram cannot pass through the cell membrane and a 10% aqueous solution was not cytotoxic towards a cell monolayer for 1 h at 37°C. Monolayers of CHO cells were given 5 or 10 ml of fresh complete medium (depth of medium 2 or 4 mm above cell monolayer), containing the necessary quantity of Biligram, 5 min before irradiation.

Cell monolayers growing on the bottom of flat plastic flasks were irradiated from above with X rays generated at 250 kVp (half value layer 0.83 mm Cu) and at a dose-rate of 1.60 cGy min^{-1}. The incident beam passed through 4 mm of iodine-rich medium before reaching the cell layer.

In a further experiment, to examine the importance of the direction of the incident beam in relation to the iodine-rich medium and cell layer, the monolayer was irradiated from below, *i.e.* the X-ray beam passed through the bottom of the dish and the cells before traversing the overlying layer of medium (2 mm deep). The dose-rate for this irradiation was 1.81 cGy min^{-1}.

The experiment was repeated with photons from a cobalt-60 source (1.25 MeV) to confirm that there is little enhancement at this energy where photoelectric absorption is minimal. In this case, cells were irradiated from above at a dose-rate of 42.1 cGy min^{-1}.

After irradiation, monolayers were washed, trypsinised and plated for cell survival. After incubation for 6 days, the colonies were fixed and stained with carbol fuchsin and then counted. A colony was defined as comprising 50 or more cells. The plating efficiency (PE) was calculated by dividing the number of colonies scored by the number of cells plated. The ratio of PEs (treated/control) is termed the surviving fraction.

RESULTS

Data were processed using the computer program designed by Gilbert (1969) for a multitarget, multihit analysis. This analysis showed that n-values for the four dose–response curves were not significantly different ($p = 0.47$, by an F test) and so data were re-analysed assuming curves of the same shape, with the constraint that all curves have a common value for n of 6.7 ± 1.2. D_0 and dose-modification factors (DMFs) are shown in Table I and the fitted curves are illustrated in Fig. 1. The DMF at the highest iodine concentration, 50 mg ml^{-1}, was 2.72. When monolayers were irradiated with 250 kV X rays from below, the DMF was 2.2 using an iodine concentration of 50 mg ml^{-1}. Thus there appears to be little difference between X rays initially traversing the cell layer or the iodine-rich layer.

As expected, Biligram in the medium had no influence on survival when irradiated with higher-energy photons (1.25 MeV) produced from the cobalt source.

TABLE I

ENHANCEMENT OF RADIOSENSITIVITY BY IODINE

Iodine concentration (mg/ml)	D_0 (Gy)	Slope ratio
0	1.25±0.05	1.00
5	1.05±0.05	1.19
25	0.67±0.03	1.87
50	0.46±0.02	2.72

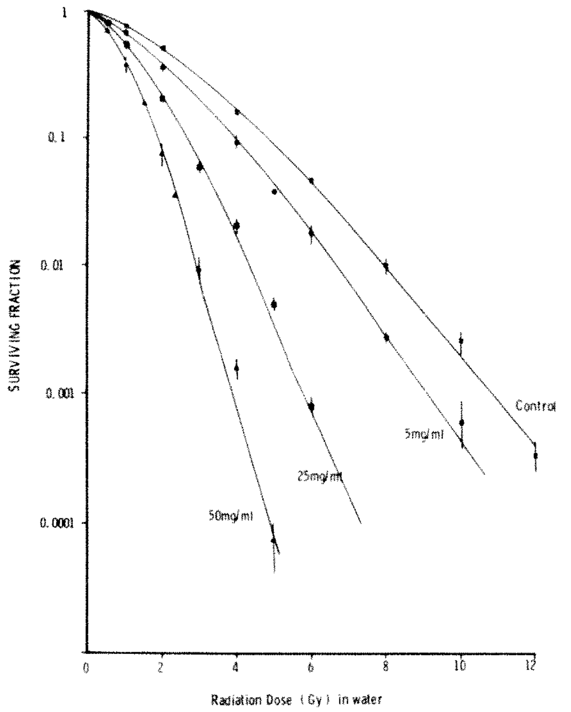

FIG. 1.

Survival curve for CHO cells irradiated with or without Biligram. Surviving fraction plotted against radiation dose in water: control (no contrast agent), x; 5 mgI ml^{-1}, ●; 25 mgI ml^{-1}, ■; or 50 mgI ml^{-1}, ▲ (iodine concentration in the culture medium during irradiation). Points are means of three replicate experiments; the vertical bars indicate the spread of data.

DISCUSSION

Irradiation of a monolayer of CHO cells overlaid with iodine-rich contrast medium (50 mg iodine ml^{-1}) resulted in an enhancement of the radiation dose by a factor of 2.72. It is of interest to determine what enhancement could theoretically be expected under these circumstances.

These experiments used an X-ray beam generated at 250 kVp. The filtration in the beam (0.54 mm Al + 0.16 mm Cu) is relatively light, giving a half value layer of 0.83 mm Cu. More than half the photons in such a beam would have energies of less than 100 keV where the mass energy absorption coefficient of iodine relative to that of water is greatest. Most of the resulting photoelectrons will have energies between approximately 30 keV and 150 keV, corresponding to ranges of 18 μm and 252 μm, respectively, in tissue-equivalent material.

Calculation of the expected absorbed dose in the monolayer of cells is complicated by the fact that they are lying on an interface and not homogeneously surrounded by the iodine medium. In the latter case one would expect a dose-enhancement factor of about four for a medium containing 5% (50 mg ml^{-1}) iodine. The fact that an enhancement factor of between two and three was obtained regardless of the orientation of the primary beam indicates that the direction of the secondary electrons which are depositing energy in the cells is not very dependent on the primary photon direction. At these energies the majority of photoelectrons will be produced in the forward direction initially, but Auger electrons will be emitted isotropically. For cells surrounded by homogeneous medium containing 5% iodine, it could be predicted from the results of irradiation from above and below that the dose-enhancement factor would be the sum of the two measured factors minus 1.0 (strictly 0.95 for a 5% medium), *i.e.* giving a value of about four. Further experiments are in progress to verify this.

These results show very convincingly that the presence of iodinated radiological contrast agents will greatly increase radiation-induced cell injury. This has implications in two spheres.

(*i*) *Diagnostic radiology*

There is already literature documenting adverse effects of the combination of contrast agents and radiation on lymphocytes (Adams et al, 1977; Norman et al, 1978; Cochran et al, 1980; Cochran & Norman, 1982). Studies on micronuclei suggest that some contrast agents (diatrizoates) may possess intrinsic mutagenic properties which are enhanced by radiation exposure (Norman et al, 1978; Cochran & Norman, 1982). Indeed, impurities belonging to known families of mutagens are found in low concentrations in commercial preparations of the diatrizoates (Weiss et al, 1981). Nelson et al (1982) have pointed out, however, that micronuclei are not specific evidence of mutagenesis, but rather, are non-specific evidence of cell injury. Furthermore, Hadaghy et al (1982) have presented evidence that the injury is due, not to the contrast agent itself, but to a synergistic effect of the contrast agent and radiation.

All these studies were performed at diagnostic energies and with diagnostic radiation doses. Our data extend this work to the orthovoltage energy range and to therapy doses. The higher energies and doses lead to the more dramatic effect of cell death. The lower photon energies of diagnostic procedures will, however, give a higher yield of photoelectrons. Consequently, it must be accepted that, because of the increased number of photoelectrons, the possibility of cell injury leading to mutagenicity/carcinogenicity may be a real one. This is yet another reason for discrimination and caution in the use of contrast agents in diagnostic radiology, perhaps particularly in patients of childbearing age.

(*ii*) *Radiotherapy*

The DMF of 2.72 was achieved at an iodine concentration of only 50 mg ml^{-1}, suggesting scope for achieving even greater gains. It clearly offers the promise of some substantial improvements in the effectiveness of orthovoltage radiotherapy. Very high iodine concentrations can be achieved in tumours by selective catheterisation and infusion of their supplying vessels. Subsequent irradiation using orthovoltage energy range photons would then be expected to increase the dose to tissue up to several microns around filled vessels, with those cells lining blood capillaries, *i.e.* endothelial cells, receiving the highest dose. *In vivo*, the endothelial cells line the three-dimensional capillary structure and any radiation beam will pass through, consecutively, an endothelial cell layer, the iodine-enriched blood and the endothelial cell layer farthest from the source of the incident beam. However, the present work shows that good enhancement could be obtained regardless of the orientation of the primary radiation beam. Destruction of the endothelial cells lining the capillaries may well result in failure of the vasculature and starvation of dependent tumour cells. Such an attack on tumours via the destruction of their vasculature has been suggested by Denekamp (1982) as an additional form of tumour therapy used in conjunction with other forms of treatment.

CONCLUSION

Radiological contrast agents are designed to increase X-ray absorption, usually by the inclusion of iodine atoms with their high photoelectric absorption. The resulting increase in absorbed dose produces greater cytotoxic effects. On the one hand, this is undesirable and explains the observation by several authors of lymphocyte damage in both *in-vitro* and *in-vivo* studies. On the other hand, it has a positive aspect, offering the possibility of a simple, safe means of increasing the efficacy of radiotherapy.

ACKNOWLEDGMENTS

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The lead apron: room for improvement?

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Improvement of the radiation protection of the wearer of a lead apron may be obtained by increasing the volume of tissue protected by the apron or by increasing the thickness of the lead apron We evaluate the merits of these two possibilities

Radiosensitive tissues include the red bone marrow, breast, thyroid and gonads. Gill et al (1980) assessed the effective dose equivalent of the body, taking those parts protected by a lead apron and those unprotected. They estimated that 63% of the weighted organs were protected and 37% were not protected

METHOD

As an indication of the efficiency of protection offered by a lead apron, an assessment was made of the amount of red bone marrow not protected by a modern lead apron (Rothband double-sided SFML with belt) The marrow distribution in each bone was taken as that assessed by Poretti et al (1981) and the marrow assumed to be evenly distributed within each bone or relevant part of a bone A horizontal beam of the scattered radiation was assumed The proportion

TABLE I

ESTIMATED PERCENTAGE OF RED MARROW PER BONE UNPROTECTED BY CONVENTIONAL LEAD APRON FROM A HORIZONTAL PARALLEL BEAM (PERCENTAGE OF TOTAL RED MARROW)

	Scapulae	Clavicles	Thoracic vertebrae	Manubrium, sternum	Humeral heads	Skull, cervical spine	Total red marrow unprotected (%)
Body build:							
small	0	75 (1.2)	42 (6.2)	100 (0 7)	50 (1)	100 (17.5)	26.6
large	25 (1.3)	50 (0.8)	33 (5 0)	50 (0.4)	100 (2)	100 (17 5)	27

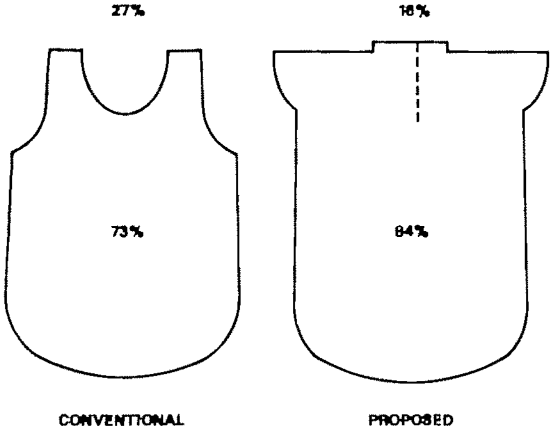

FIG 1.

Conventional and proposed lead aprons. Figures show percentages of bone marrow shielded and unshielded.

of bone exposed was determined by direct observation (Table I). The body build made little difference to the proportion of marrow exposed, taking as examples large and small builds of people; the different bones were exposed to varying degrees. We estimate that although 73% of the red marrow was protected, 27% was not.

A calculation was then made of the proportion of marrow similarly exposed if a lead apron wholly protected the pectoral girdle, humeral heads, sternum, thoracic spine and the lower third of the cervical spine (Fig. 1) In such a situation, 84% of the red bone marrow is protected and 16% not.

The attenuation of scatter from diagnostic X rays is known (National Council on Radiation Protection, 1976). An estimate of the marrow dose can be made for various combinations of apron and thickness of lead (Table II), using the figures for scatter generated at 100 kVp

TABLE II

COMPARISON OF THE DOSE RECEIVED WEARING CONVENTIONAL AND NEW APRONS OF DIFFERENT LEAD EQUIVALENT THICKNESS, EXPOSED TO A BROAD HORIZONTAL 100 KVP BEAM

Lead equivalent (mm)	Dose* (no lead apron = 100 units)	
	Conventional apron	Proposed new apron
0	100	100
0.1	27+19 = 46	16+22 = 38
0.25	27+3.1 = 30.1	16+3.6 = 19.6
0.35	27+1.9 = 28.9	16+2.2 = 18.2
0.5	27+1.02 = 28	16+1.18 = 17.2
1.0	27+0.2 = 27.2	16+0.24 = 16.2
2.0	27+0.001 = 27	16+0.002 = 16
3.0	27+0.0001 = 27	16+0.0001 = 16

*Dose is skin dose (100) × % unprotected marrow + attenuated skin dose × % of covered marrow.

DISCUSSION

The calculations made are based on exposure to a wide horizontal beam using uniform exposure throughout the body. In practice this is not the case since the scatter from a patient varies, depending on the angle from the source (Faulkner & Moores, 1982) and the distance of the different parts of the wearer from the source of the scatter. In addition, there is usually primary protection, *e.g* a lead curtain between the patient and the wearer, and, even in a uniform field, different parts of the red bone marrow will receive different radiation doses due to the different thicknesses of overlying tissue (Poretti et al, 1981) In practice, however, these factors should not significantly alter the conclusion that a gown with a wider shoulder and higher neckline would afford improved protection. A further 10%, approximately, of red marrow would be protected by an apron whose neckline was 12 cm higher and shoulders 6 cm wider than a conventional apron. This proposed apron would also cover the thyroid, which is a significant organ with regard to radiation carcinogenesis. The arm holes should be smaller than at present to ensure that, for women, the lateral breast is covered. We prefer an anterior velcro neck fastening about 25 cm from the top. This allows easy access for the head and closes firmly in wear The back should mirror the front, except for a slightly lower neckline. One side should be continuous back and front, the other side open, so that the apron can be put on, and closed with velcro. Such an apron has been in use for some years and is most comfortable to wear.

This proposed apron offers more protection than a conventionally shaped apron. Indeed a "new" apron of 0.25 mm lead equivalent offers more protection than a conventional one of infinite thickness. Many aprons in current use are of 0.35 mm lead equivalent The price of aprons is to a large degree related to the lead content. We would, therefore, expect the "new" apron, if it is 0.25 mm lead equivalent, to cost less than a conventional apron of 0.35 mm, as well as offering better protection. It would also weigh less, adding to the comfort of the wearer.

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ADDENDUM

As W. S Rothband & Co are the only manufacturer mentioned above, they have asked us to make the following points·

Other manufacturers make similar gowns to the Rothband doubled-sided SFML, which is made to conform to British Standard BS3783. Rothbands also offer a Polycoatee gown which does give better coverage than the conventional gown described above, and they now offer examples of the design proposed in this communication.

1987, *The British Journal of Radiology*, *60*, 205

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

TLD patient monitoring

THE EDITOR—SIR,

Thermoluminescent dosemeters (TLDs) provide a valuable means of measuring dose distributions in clinical practice A problem arises, however, in handling, labelling and positioning the individual dosemeters, which must be kept as clean as possible at all times. Commonly, the dosemeters may be wrapped and sealed in plastic sachets and taped to the target position, but this is a tedious process which may be difficult to control precisely.

At Mount Vernon Hospital, TLDs are routinely used for eye dose measurements and holders have been prepared which permit the rapid and precise positioning of the dosemeters with a known thickness of build-up material. These have been prepared from clear acrylic, curved to fit neatly on the eye, like an external eyeshield. A small size has a nominal diameter of 20 mm and a large size, a nominal diameter of 25 mm The outer surface of the holder is inscribed with an arrow to mark the superior, and an R or L to identify the orientation The back surface carries a channel cut into the acrylic 3 5 mm wide, and 1 mm deep The length of the channel is 10 mm in the smaller holder and 18 mm in the larger holder. These channels permit the precise placing of TLD chips in sequence across the holder The front surface of the channel consists of 2 mm of acrylic The chips are finally held in place by a cover-slip held by sticking tape

Loading and unloading is quick and precise, positioning is unambiguous and the holders are reusable and easily cleaned. The system is currently being extended with a selection of flat, numbered holders for use in general dosimetry. A selection of insensitive filling strips is also used when less than the full complement of dosemeters is required. Extra build-up material, if necessary, may be added easily and precisely.

Yours, etc ,
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(*Received August 1986*)

Amersham afterloading system

THE EDITOR—SIR,

The Amersham afterloading system is now a widely used technique for delivering intracavitary radiotherapy treatment. The equipment and method have been described in a number of papers, including Bateman et al (1983).

A typical treatment will call for the positioning of an intrauterine applicator tube and two ovoid applicator tubes in the patient. Currently these tubes are identified by the numbering of the ovoid tubes "1" or "2" on their shafts. For speed and convenience, when the source trains are loaded or unloaded, rapid identification of the individual tubes is desirable

Experience has shown that the ovoid applicator tube numbers are not infrequently difficult to identify when in the patient if they are rotated to an aspect other than the anterior. It is suggested that speed and convenience would be enhanced if the identifier tags "1" and "2" were replaced by a single or a double band on the shaft. Identification would then be immediate from any aspect.

Yours, etc ,
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REFERENCE

BATEMAN, T J., DAVY, T. J & SKEGGS, D. B. L., 1983. Five years' hospital experience with the Amersham caesium-137 manual afterloading systems. *British Journal of Radiology*, *56*, 401–407

Book review

Double Contrast Examination of the Colon (Principles and Practice). By A. Weissman, M Clot and J. Grellet, pp ix+165, 1985 (Springer-Verlag, Berlin), DM115.
ISBN 3–540–15334–9 (Germany)
0–387–15334–9 (USA)

Although this is a relatively slim volume, reminiscent of Welin's monograph on double-contrast radiology of the colon, it is a book full of interest and information to the practising radiologist, by which I mean all radiologists, from the complete novice to the most experienced The reason is that the text contains many points which one often takes for granted and yet are not readily seen in print This particularly applies to the introductory chapters, which contain a very detailed account of the preparation for, and the interpretation of, double-contrast barium enema examinations The relationship of posture to radiographic image is usefully discussed, as are all the causes of artefact and false image.

The authors are obviously complete devotees of the double-contrast technique, as witness their statement "The double contrast barium enema should, except where contraindicated, replace the traditional barium enema" This comment is made in relation to polyp detection, which is one of the most important reasons for performing a barium enema

The following chapters deal in the standard way with all the common diseases affecting the colon. In some areas the text, together with accompanying line diagrams, is perhaps a little too detailed, such as the discussion on primary colo-rectal carcinoma. Here the formation of the X-ray image is considered in minute detail and I am not sure that it is all necessary. This, however, is a small quibble and must not detract from the overall merits of the book. Its other great strength lies in the quality of the illustrations, which, true to the Springer-Verlag tradition, are superb. These are accompanied by informative legends, and all the lesions are clearly demonstrated.

I find little to fault in this publication. I believe that it should be read by everyone training in radiology and the more experienced can learn much from it. At DM115 it might prove expensive for individual purchase, but I am certain that it should be found on the library shelves of all radiology departments.

A FREEMAN

1987, *The British Journal of Radiology*, 60, 207–208 FEBRUARY 1987

Proceedings of The British Institute of Radiology

Safety of diagnostic ultrasound

Abstracts of papers presented at the joint meeting with The British Medical Ultrasound Society, The College of Radiographers, The Institute of Physical Sciences in Medicine, The Royal College of Obstetricians and Gynaecologists, The Royal College of Radiologists and The Royal Society of Medicine, organised by The British Institute of Radiology and held at the Edward Lewis Lecture Theatre, Middlesex Hospital Medical School, London W1 on Thursday, May 15, 1986

Chairman: H. B. Meire

Mechanisms for the biological effects of ultrasound, by Dr G. ter Haar
Exposure conditions in diagnostic ultrasound, by Dr F. A Duck
Biological research at diagnostic ultrasound exposures, by Dr A J. Mortimer
Epidemiological aspects of diagnostic ultrasound, by Dr P A. McKinney

MECHANISMS FOR THE BIOLOGICAL EFFECTS OF ULTRASOUND

Gail ter Haar

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There is inadequate knowledge of the precise mechanisms by which ultrasound interacts with tissues to produce biological effects In the absence of verifiable evidence for damage caused by diagnostic ultrasound, it is important that these mechanisms be properly understood, and exposure levels set at which each becomes important, in order that intelligent assessment may be made of the effect of any given medical ultrasound exposure on human tissue

As an ultrasonic beam travels through tissue, some of its energy may be absorbed, thus raising the tissue temperature. The resultant temperature is unlikely to be significant biologically for pulsed diagnostic exposures Another mechanism by which ultrasound can produce changes in biological media is by cavitation. This is the formation, growth and activity of microbubbles Significant shear stresses may be set up near oscillating bubbles In suspension cultures, the activity of these cavitation microbubbles may be sufficient to lyse cells The presence of cavitation in opaque, intact mammalian tissues is difficult to detect, but has been demonstrated following therapeutic ultrasound exposure conditions The exposure conditions necessary for microbubble formation may be investigated using agar-gel phantoms. This allows acoustic pressure threshold determination for a range of pulsing regimes and ambient temperatures

There exist also some interaction mechanisms that are neither thermal nor cavitational in origin One of the most important is acoustic streaming. Shear stresses may be considerable where acoustic streaming is present, and these may lead to membrane damage or changes in membrane permeability

EXPOSURE CONDITIONS IN DIAGNOSTIC ULTRASOUND

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The characteristics of acoustic fields which are generated by transducers used with diagnostic ultrasound equipment can now be measured with some accuracy Ultrasonic force balances have been designed which measure acoustic powers in the milliwatt range in both pulsed and continuous beams. Polyvinylidene difluoride (PVDF) membrane hydrophones, available commercially, allow the direct measurement of the pressure waveform generated in water These devices may be calibrated against standards at the National Physical Laboratory to allow accurate measurements to be carried out locally The broad-band frequency characteristic of the PVDF hydrophones allows the observation of the substantial finite amplitude distortion which may occur in diagnostic pulsed fields Intensity values, time-averaged over pulse length, pulse repetition period, or frame repetition period can be derived from the hydrophone measurements

A survey of overall peak exposures from imaging equipment has shown total powers in the range 0.5–80 mW, and peak pressures in the range 0 1–7.4 MPa (positive) and 0 1–3.9 MPa (negative) Spatial-peak intensities lie in the range 0.4–1100 W cm^{-2} (Isppa), and time-average intensities for scanning systems 0.02–37 $mWcm^{-2}$ and for M-mode 1 6–680 mW cm^{-2}. Pulsed Doppler pulse lengths overlap those used for imaging, but the higher pulse repetition frequencies gave higher values of Ispta, in the range 71–825 mW cm^{-2}. Continuous wave Doppler units for cardiovascular applications gave Ispta in the range 11–455 $mWcm^{-2}$ where those associated with scanners were at the upper end. Using the AIUM statement on safety, units operating at the upper limits of intensity should be used continuously for no more than about 1 min. The pressures measured in water have been reported to be sufficient to generate cavitation and free radicals in pulsed fields at 1 MHz. While soft-tissue attenuation will reduce those acoustic values *in vivo*, there will be some circumstances, especially in uterine scanning, where much of the acoustic path will be through low-loss fluids, and the attenuation may be no more than 3 dB.

BIOLOGICAL RESEARCH AT DIAGNOSTIC ULTRASOUND EXPOSURES

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The experimental study of the biological effects of diagnostic ultrasound is limited by two major factors. The first is that any effect which does occur is very subtle when observed in the short term The second and more important is that the mechanisms of action of ultrasound are not sufficiently well understood to allow prediction of the most appropriate experiments The recent proliferation of diagnostic instruments with increasingly higher acoustic output, some extending into the range of average intensities where bioeffects have been observed, has heightened the importance of being able to make some predictions from the disorganised bulk of experimental data which have been reported. Results on cells in suspension have shown altered sister chromatid exchange. These results have not been reproduced consistently and the meaning with respect to human biology is unclear. More important is the observation of alterations in the cell surface affecting proliferation and transformation. Results of experiments on animals have shown a slight weight reduction in offspring, which may be attributable to ultrasound exposure. In addition, recent studies have shown a decrease in fertility after exposure to ultrasound. Experimental results to date have not demonstrated any hazard which would limit the prudent use of diagnostic ultrasound.

EPIDEMIOLOGICAL ASPECTS OF DIAGNOSTIC ULTRASOUND

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Epidemiology studies the environmental causes of human diseases based on observations of human populations. The outcome of such studies are to quantify associations between hazard and disease, usually measured in terms of risk estimates which infer cause and effect. In medicine, ultrasound (US), particularly as a diagnostic tool, has unquestionable value, but it remains a putative risk factor for both staff and patients and evaluation of its safety must be considered. Assessment of any hazardous effects must be made on human subjects as an adjunct to demonstrating bioeffects in the laboratory.

Ultrasound is generally applied following some clinical indication but, in obstetrics, diagnostic US has become a routine procedure for two apparently normal healthy patients—mother and fetus. Considering the widespread use of scanning in pregnancy, relatively few epidemiological studies have assessed any inherent risks. Researchers have examined the public health "benefits" of scanning as related to improved patient management and perinatal outcome. These indicate decreases in morbidity and mortality, particularly in high-risk pregnancies (Bennett et al, 1982; Eik-Nes et al, 1984; Bakketeig et al, 1984; Cochlin, 1984). Results may be considered equivocal with regard to routine use of US in low-risk pregnancies (Neilson et al, 1984). Statistical techniques of evaluation have demonstrated that scanning is an accurate, feasible procedure with both sensitivity and specificity.

Determination of possible fetal risks is influenced by which outcomes or end-points are selected for measurement. These could include congenital malformations or the alteration of physiological functions such as impaired nerve conduction (*e.g.* Stark et al, 1984). The very large numbers required statistically to demonstrate an effect causes major difficulties (National Council on Radiation Protection and Measurements (NCRP) 1983; National Institutes of Health (NIH), 1984), especially in attempts to measure a changing rate in an already rare spontaneous event. Published data generally fail to reveal any gross detrimental effects of obstetric US, but very rare excesses may remain undetectable.

In summary, no epidemiological studies have provided serious evidence of any hazardous effects of obstetric US. In the future, large and statistically more powerful studies will be necessary, but major limitations are "sample size" and the absence of women unexposed to US in pregnancy to act as a comparison group. Documentation difficulties will also hamper future research with the absence of "dose" records. However, it could be argued that low-key surveillance of current practice would facilitate implementation of future research.

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BIR Bulletin

February 1987

BIR sponsored visit to Institut Gustave-Roussy, March 1986

It had been a long-held ambition to see radiotherapy practice in the city where the Curies discovered radium (Reid, 1974). So, in late March, 1986, with the introduction and help of the BIR, the generous support of the European Association of Radiology and the kind invitation of Professor M. Tubiana, I visited Professor Chassagne's radiotherapy department at the Institut Gustave-Roussy (IGR), which lies in the suburbs south-east of Paris. This institute, the largest of 20 centres dedicated to cancer treatment and research in France, was named after Professor Gustave Roussy, who founded the first specialised cancer treatment clinic in 1921 nearby at the hospital Paul-Brousse After the war, General de Gaulle authorised the development of the "Centres de Lutte Contre le Cancer"; the present 15-storey hospital was opened in 1980 and treats 7000 new cancer cases a year. The multidisciplinary team approach is fully exploited and every new patient is seen by a committee of surgeon, physician and radiotherapist specialising in a particular anatomical site for a decision on the treatment programme. The treatment, where possible, follows a set protocol which allows for the continued evaluation of treatment regimes. This approach provides an excellent assessment and patients come from all over Europe and North Africa for opinions. However, it does inhibit the doctor–patient relationship.

Radiotherapy is supervised by the relevant group of specialist radiotherapists who, with the relevant committee, will assess and follow-up the patient The radiotherapy department is in two sections, external beam and "curietherapie" which deals with the brachytherapy and interstitial work. This department is world famous and was developed with Professor B. Pierquin, who has told the history of curietherapy in his Klaus-Breuer lecture (Pierquin, 1982).

The radiotherapy training for doctors is four years, which they may commence after their internship. At IGR the first two years would be spent learning the radiotherapy techniques of all the specialties. The trainee plans the treatment for all the new patients, deciding on the treatment volume with simulator films which are then checked by port films taken on the treatment machine. The physicists provide the dosimetry and at the daily "réunion technique" the senior staff of the section will comment on and amend the treatment volume and decide on the dose distribution before treatment. It is a lengthy procedure but clearly provides a good grounding in technical skills for the apprentice. The final two years will be spent in more clinically active positions, including experience with chemotherapy. While there are examinations to be taken during the training period, there is no nationally organised diploma At the end of training the equivalent British doctor is slightly more senior and will have had more clinical experience and responsibility.

Breast cancer

The French pioneered the use of conservation techniques for breast cancer (Baclesse, 1949). At IGR they have systematically shown that early breast carcinomas T1a can be controlled with lumpectomy and external beam irradiation giving comparable local control to mastectomy. An important point of note is that they have selected their patients at the time of excision biopsy on the basis of the pathologist's measurement of the macroscopic diameter of the tumour Most other groups quote tumour size on the basis of clinical measurement: it would be of interest to know how the two measurements correlate.

The experience to date has shown that breast tumours of macroscopic size up to 20 mm can be controlled with external beam therapy alone (Sarrazin et al, 1984). The whole breast receives 45 Gy in 18 fractions over 33 days. The primary site is then boosted with either a small wedged pair of fields on cobalt-60 or a direct electron boost of 15 Gy in six fractions. The local recurrence rate at five years was 5% for the conservation group and 12% for mastectomy patients (the differences are not significant). The cosmetic results were judged excellent in 32% and good in 60% of patients Because of these results the group has extended the technique to include tumours of macroscopic size up to 25 mm.

This group of tumours represents only a small percentage of breast cancers and, while at one end of the spectrum it may be possible to treat some of these tumours by lumpectomy alone (Peters, 1977), it is recognised that larger tumours would need a higher dose to the tumour bed (Arriagada et al, 1985) which may be the limiting factor in a solely external beam technique. Therefore to give a total tumour-bed dose of

65–70 Gy may be best undertaken by an interstitial technique such as that developed with iridium wire for optimum cosmetic and local control (Harris & Hellman, 1983, Pierquin & Huart, 1985). Continued studies will hopefully guide us as to where the transition point is for radiation dose and technique but, to date, this appears to be around 25–30 mm macroscopic tumour diameter for solely external beam techniques.

The place of axillary nodal irradiation in patients who have had a positive nodal biopsy has changed as a result of the experience at IGR. While there was a slightly lower incidence of local recurrence (not significant) in patients with axillary nodal irradiation, the complication rate in patients who did have axillary radiotherapy was significantly higher, 24% versus 10%, and included one case of brachial plexus neuropathy (Rawlings et al, 1983). A review of the radiotherapy technique for supraclavicular and axillary radiotherapy at Gustave-Roussy demonstrated that there was some overlap between the anterior supraclavicular field and the posterior axillary field which may have produced a 20–30% dose increase in the region of the brachial plexus. This retrospective review identified an incidence of 1–4%, depending on technique and fraction size. This has led to a revision of the technique and a policy of not irradiating the axilla if the nodal sampling is negative or if complete surgical removal of the axillary contents has been performed.

The value of irradiation of the internal mammary chain (IMC) remains controversial. Clinical problems due to recurrence in the IMC are low (3%). However, data from IGR have shown that patients with internal or medial tumours had prolonged disease-free survival after surgery or radiotherapy to the IMC compared with patients not treated in this area (Tubiana & Sarrazin, 1980). Further analysis of these data is underway as it challenges current thinking and other studies showing that radiotherapy has no effect on survival in breast cancer (Fisher et al, 1985).

One of the few studies to show a positive result with adjuvant immunotherapy in operable breast cancer has been performed at IGR (Lacour et al, 1984). Operable tumours T2–T3 (3–7 cm) were treated by mastectomy and axillary node sampling followed by post-operative irradiation when the sampling proved positive. At eight years' follow-up, the group receiving six weekly injections of polyadenylic-polyuridylic acid (which stimulate interferon production) post-operatively show a significant survival advantage ($p < 0.05$) with the subgroup of patients with one to three axillary nodes showing the most advantage ($p < 0.05$). It will be interesting to see whether this trend is maintained in longer follow-up data on this group.

Finally, for advanced disease, alternate chemotherapy and radiotherapy has been proposed in an integrated schedule (Tubiana et al, 1985). This approach is currently being assessed in cases of locally advanced carcinoma of the breast (T4b) using chemotherapy with two sessions of 25 Gy radiotherapy to the breast. The group has recently reported encouraging results with this scheduling in small-cell carcinoma of the lung.

Gynaecological cancer

In gynaecological cancers, similarly, IGR have developed combined modality techniques in an attempt to improve results. In early cervical cancer (T1 and T2A) patients have received pre-operative intracavitary radiotherapy of 60 Gy (see *ICRU Report 38,* "Dose and volume specification for reporting intracavitary therapy in gynaecology") before having a Wertheim's hysterectomy six weeks later. Histology of the cervix has shown eradication of the tumour in 85% of cases, and assessment of the pelvic nodes means that only about 20% of patients with involved nodes require further pelvic radiotherapy after surgery. While six weeks may seem a long interval for the patient to wait, the surgeons have found the time optimal with respect to the recovery of normal tissues and have not seen any increase in surgical complications.

Although there has not been a prospective study performed, the combined approach in Stage I cases has given improved five-year results compared with radiotherapy alone (83% compared with 74%), which supports a recent paper in the *British Journal of Radiology* arguing the case for combined modality treatment (Wiernik, 1986).

Similarly, they have directed themselves to the controversy as to the place of combined treatment in endometrial carcinoma (Gerbaulet et al, 1985). They have maintained the role of pre-operative radiotherapy, but only to the vaginal vault, which is achieved utilising two vaginal sources positioned in individually made vaginal moulds, as are all their intracavitary treatments. This approach, giving 60 Gy at 0.5 cm to the vault, is followed by immediate surgery, so the combined procedure is achieved on one hospital admission for the patient. The pathologist can thereafter fully assess the depth of myometrial invasion, unaffected by intrauterine irradiation and the state of the pelvic lymph nodes, the results of which determine whether any post-operative pelvic radiotherapy is indicated. Thus for Stage I cases, treatment is complete after surgery and, for the more advanced cases, whole pelvic radiotherapy can be performed with only vaginal-vault shielding. This approach is also supported by the finding that in Stage I cases the complication rate was higher when vault radiotherapy was given post-operatively (17% compared with 3%), which is thought to be because of the increased likelihood of bowel being adherent in the pelvis and, in particular, to the vaginal vault. In their series of 151 patients (Stages I and II) the vaginal-vault recurrence rate was 1.4% (15% without radiotherapy in historical series) and pelvic recurrence rate 3.5%. The five-year survival rates were Stage I, 92%, Stage II, 84%.

In advanced cervical carcinoma, several approaches have been examined. A pilot study with misonidazole (Ginaski et al, 1985) showed encouraging local control and three-year survival rates when compared with historical controls, and, although the Medical Research Council study failed to show any benefit, the potential combination of the new generation of hypoxic cell sensitisers with higher pelvic doses as given in this study gives some reason for optimism in this field.

A feasibility study in 36 patients with advanced cervical carcinoma showed no survival benefit using chemotherapy, cis-platinum and cyclophosphamide alternating with three separate radiation sessions of total dose 60 Gy by external beam and intracavitary techniques. Three patients who had small-bowel injury are being evaluated further.

Like several other groups (Minton et al, 1986), IGR has been exploring the feasibility of using whole-abdominal radiotherapy in cases of advanced carcinoma of the ovary (Stages III and IV) who, following surgery and chemotherapy, have no or minimal (⩽ 2 cm) residual intra-abdominal disease. They have used a dose of 20 Gy with good tolerance, but we will have to wait for a randomised prospective study to determine whether this radiotherapy contributes anything to the overall survival of the group

I have not mentioned the extensive interstitial work undertaken in the department of curietherapy for head and neck cancers as this was fully described in a previous report (Williams, 1985).

I hope that I have been able to give a glimpse of some of the varied work going on at the IGR. I am most grateful to Professor Chassagne and his colleagues who organised my programme and enabled me to have such a rewarding visit

MICHAEL MINTON

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Press release

EULIMA: project for a European medical accelerator

At the European Organisation for Research and Treatment of Cancer (EORTC) meeting held in Nice, October 18–19, 1985, the idea of a European light-ion medical accelerator (EULIMA) was proposed. On March 14, 1986, a group of potential medical users, radiobiologists, physicists and accelerator engineers from different European countries met at CERN to define the goals of the project and to examine the possibility of a feasibility study. A request for funding for such a study was made to the European Economic Community

A meeting held at CERN in November 1986 then initiated the feasibility study by setting up the project committee and a scientific council. More precise recommendations for the accelerator design were also produced

The possible therapeutic advantages of high-energy charged particles have been recognised earlier and a series of biomedical experiments have been carried out at the BEVALAC accelerator in Berkeley Biomedical accelerators for light ions designed for clinical treatment are now proposed by the National Institute of Radiological Sciences (NIRS) at Shiba, Japan and by the Lawrence Berkeley Laboratory (LBL) in the USA (light-ion biomedical research accelerator, LIBRA)

The EULIMA concept

The key concept of EULIMA is the introduction of the advantages of light-ion treatment in an operational medical facility The EULIMA accelerator incorporates (i) an existing compact cyclotron used for neutron and proton therapy in the energy range of 60 MeV (like MEDICYC in CAL Nice, France or CYCLONE in CRC Louvain-la-Neuve, Belgium) and (ii) a booster that accelerates the particles injected from the cyclotron to a final energy of several hundred MeV/nucleon. Preliminary studies being carried out show that a cyclotron, suitable for a hospital, consisting of four separate sectors and a single circular superconducting coil could reach a maximum energy of about 400 MeV/nucleon.

BIR Radiation Protection Committee comments on the COMARE Report

The Committee on Medical Aspects of Radiation in the Environment (COMARE) was set up to implement some of the recommendations of the Black Committee report on the incidence of leukaemia in Seascale The intention appears to have been to widen the terms of reference and the area covered by the enquiry but, in the event, the emphasis in its first report is heavily on the area immediately around Sellafield, and in fact the COMARE report appears to be an extension of the Black report, with which it is highly convoluted

Both the introduction and the first few pages of Chapter 2 of the first COMARE report are so loaded with carefully worded disclaimers that it is not surprising that the general public, steeped in the hyperbole of newspaper reporting, views scientific reports such as this with a great deal of suspicion

The COMARE report attaches great significance to a report from Dr Jakeman, a scientist who had worked at Sellafield from 1954 to 1956, based on his recollection of events at the time. The question must be faced as to what impact such suggestions as are now made about the magnitude of unplanned discharges to the environment would have in an area of uncertainty. Either (a) the report containing these figures was submitted in 1956 and ignored or suppressed or (b) the report did not contain these figures expressed in an unambiguous manner.

An important point is raised in Paragraph 3 20, namely that the reason why the suggested 50-fold increase in the estimated release of uranium oxide in 1954/55 resulted in only a two-fold increase in the dose to red bone marrow to the 1950 cohort was because the original estimation of this dose was based partly on the sparse environmental monitoring carried out at the time and not on the reputed discharge. Also, part of the increase in the high linear energy transfer (LET) component is because the National Radiological Protection Board now consider that radioactive material is transferred twice as efficiently from the gut into the body as was previously believed

However, the really surprising fact emerges in Table 4 that, even when high-LET radiation is taken into consideration, the discharges from Windscale and Sellafield, even in the worst period of their history, produced an increase of only 65% over natural background. Nevertheless, as Paragraph 4 11 points out, there is an apparent excess incidence of leukaemia in Seascale, which might have arisen because of any one of four factors, two known and two unknown. It is suggested that the excess may well have been caused by some combination of two or more of these factors

The COMARE Committee finds no evidence which connects radiation with this incidence of leukaemia. It will never be known what the magnitude of the discharges was nor, therefore, what the population doses were, and yet in spite of the opportunity presented by the publication of this report, the Committee still sits on the fence with regard to the implications of the Sellafield discharges.

Crown immunity

As a result of a debate in the House of Lords which took place on Wednesday, October 15, 1986, an amendment was moved which has the effect that the protection of Crown immunity was removed from Crown establishments, such as hospitals within the National Health Service

While Crown immunity has never applied to individuals, and many institutions have already waived their rights to immunity and some actually invite the inspectors of the Health and Safety Executive to visit their premises, there may be others who will be affected by this change.

The effects of the amendment are that inspectors may impose either improvement or prohibition orders on premises or situations which are unsatisfactory and that they may prosecute in serious cases of personal or corporate liability While such prosecutions are unlikely, the adverse publicity following the imposition of an improvement or prohibition order would be extremely undesirable, and the resultant odium would have lasting and unpleasant consequences for the individuals and departments involved, particularly in the case of incidents involving the use of sources of ionising radiation, where the RPS and the RPA might be implicated

RADIATION PROTECTION COMMITTEE

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and is expected to include.

The BIR Mackenzie Davidson Memorial Lecture, by Professor M J Peckham, "The clinical biology of testicular germ cell tumours"

The BIR Mayneord Lecture (sponsored by 3M UK plc), by Miss Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"

The RCR George Simon Lecture, by Sir John Batten, "Radiology and cystic fibrosis"

The BIR Presidential Address, by Professor R J Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2

For further information and registration forms please apply to the Assistant Secretary Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085)

The BIR Nycomed Scandinavian Scholarships 1988

The British Institute of Radiology invites applications for the 1988 Nycomed Scandinavian Scholarships These Scholarships, which are generously funded by Nycomed (UK) Ltd, enable United Kingdom diagnostic radiologists, preferably members of the British Institute of Radiology, to visit Scandinavian academic departments for up to two months' concentrated study, free of financial constaints (a maximum of £2500 per month will be provided).

For further information please write to The General Secretary, The British Institute of Radiology, 36 Portland Place, London W1N 4AT.

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Radionuclide Investigations of the Lung
February 11, 1987
Joint IPSM/BIR (Nuclear Medicine Subcommittee) all day meeting organised by IPSM.

All day non-topic proffered papers meeting
February 13, 1987 at 9.30 a m.
Chairmen. Dr W. A Cramp, Dr N. J. McNally, Professor R. J. Berry and Dr J. W. Hopewell.
Joint ARR/BIR (Radiobiology Subcommittee) meeting organised by the Association for Radiation Research.

Picture Archiving and Communications Systems
February 25, 1987 at 9.45 a.m
Middlesex Hospital Medical School, London
Chairman: Professor I. Isherwood
Speakers: Dr O. Craig, Mr D Rothery, Dr C. Taylor, Dr W Lees, Mrs J E. Burnett, Dr R. Rupprecht, Professor L Gillanders, Mr H. Griffith, Mr P. Vernon, Mr C. Robertson, Mr J Tiemann and Dr C. Greinacher
Topics will include image display, image transmission and image storage.
All day meeting organised by Industry Committee.

Annual General Meeting
May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy
May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Topics are expected to include integrated treatment planning, special imaging techniques, radiotherapy portal imaging, three-dimensional imaging and simulator CT.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione
May 20, 1987
Royal Naval College, Greenwich

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p m, and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Use of RSM Library

A reciprocal agreement has been set up to allow BIR members limited use of the RSM Library for reference purposes. Members wishing to do so should apply to the BIR librarian for a visitor's card. BIR members using the RSM Library will have access to photocopy and online services on a cost-recovery basis.

The RSM Library is situated at 1 Wimpole Street, London W1M 8AE and is open weekdays 9 a m. to 9.30 p.m, Saturdays 10 a m to 5 p m Its collection of medical books and journals is very large

Recent additions to the Library

BJR Supplement No. 19: Radiation damage to skin, fundamental and practical aspects. Proceedings of a workshop held in Saclay, France, October 9–11, 1985

Turner, J. E.: Atoms, radiation, and radiation protection. 1986

Watmough, D. J. & Ross, W. M. (Eds): Hyperthermia. 1986

Scientific documents

World Health Organisation: *Updated background information on the nuclear reactor accident in Chernobyl, USSR* Information received on public health measures as of 12 June 1986 from members states, Canada, USA and the CEC. (Meteorological data, information on levels of contamination and other matters are not included in this text.) Final issue. Also updated summary of data situation with regard to activity measurements 12 June 1986. Final issue.

World Health Organisation, Regional Office for Europe *Summary review of measurement results relevant for dose assessment relating to the Chernobyl Accident.* Updated revision No. 7. Final issue

BSI 86/22570. European Standard. International Electrotechnical Commission. IEC Standard. CISPR 22. 1st edit. 1985 Draft prEN 55 022, copyright CENELEC 1986. *Limits and methods of measurement of radio interference characteristics of information technology equipment.* CISPR 22 (1985—1st edit)

These documents are now filed in the Library.

Hire of Institute facilities

Readers are reminded of the availability for hire of the Lecture Theatre, Foyer and Library. Affiliated societies are offered a discount.

The Lecture Theatre holds up to 100 people in raked seating and has excellent audio-visual equipment, including VHF video. The Foyer provides space for registration and refreshment breaks for 40 people. The Library, with its beautiful Adam ceiling, can accommodate up to 75 people for refreshment breaks or for an evening reception.

Members' use of the Toshiba Room

Members may borrow the Toshiba Room free of charge, subject to availability. This conference meeting room seats 16 people with comfort.

Full details from Mrs Anne Clayton, Assistant Secretary: Administration at the BIR.

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1 75 per printed line, per insertion. Please contact the Managing Editor

Radiation Transport Calculations Using EGS4
February 16–19, 1987
Ottawa, Canada
Further details. D W O. Rogers, Physics Division, NRCC, Ottawa, Ontario K1A 0R6, Canada (Tel 613-993 2715)

Computed Body Tomography 1987: the cutting edge
March 5–8, 1987
Peabody-Orlando Hotel, Florida, USA
Further details Program Co-ordinator, Office of Continuing Education, Turner 22, 720 Rutland Avenue, Baltimore, Maryland 21205, USA (Tel. 301-955 5880).

Breast Imaging Update
March 7–8, 1987
San Francisco, USA
Further details. Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Avenue, San Francisco, CA 94143-0628, USA (Tel. 415-476 5731)

30th Annual Diagnostic Radiology Postgraduate Course
March 9–13, 1987
San Francisco, USA
Further details. Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Avenue, San Francisco, CA 94143-0628, USA (Tel 415-476 5731).

Perspectives in Radioprotection
March 13–14, 1987
Bethesda, Maryland
Further details. Dr Joseph F Weiss, Armed Forces Radiobiology Research Institute, Bethesda, MD 20814-5145, USA

Contemporary Trends in Diagnostic Nuclear Medicine
March 14–15, 1987
San Francisco, USA
Further details. Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Avenue, San Francisco, CA 94143-0628, USA (Tel 415-476 5731).

London Course in Whole Body Computed Tomography
March 15–19, 1987
Gleneagles Hotel, Auchterarder, Scotland
Further details Mrs J O'Donnell, Organising Secretary, Department of Radiology, Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT

Ultrasound Update
March 18, 1987
Hillingdon Hospital, Uxbridge
Course organiser Dr Dez Shirley
Further details Postgraduate Administrator, Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN (Tel. 0895-37964 or 38282 ext 253).

1987 European Workshop on Magnetic Resonance in Medicine
March 26–27, 1987
University College, London
Further details Conference Secretariat, Magnetic Resonance in Medicine 1987, c/o Institute of Physical Sciences in Medicine, 47 Belgrave Square, London SW1X 8QX.

British Nuclear Medicine Society Annual Congress
April 12–15, 1987
Imperial College, London
Further details Mrs A Taylor, BNMS Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP

The Finzi Lecture
April 15, 1987
Royal Society of Medicine, London
"The solitary pulmonary nodule" by Dr S Segalmann
Further details Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE.

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details Secretariat ECR '87, SPRMN, Av Elias Garcia, 123-7° DTo, 1000 Lisboa, Portugal, (Tel 77-05 30, Telex 62074 SPRMN P)

Radiology of the Small Intestine
June 12, 1987
John Radcliffe Hospital, Oxford
Further details. Dr D. J. Nolan, Dept of Radiology, John Radcliffe Hospital, Oxford OX3 9DU (Tel. 0865-817 238)

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel 01-935 5726, ext. 206)

St Bart's Megavoltage Radiotherapy 50th Anniversary Conference
September 3–5, 1987
St Bartholomew's Hospital, London
Further details The Secretariat, Concorde Services, 10 Wendell Road, London W12 9RT

Radiology in Yorkshire
September 13–20, 1987
Harrogate, Yorkshire
Further details: D. Beatty Crawford, M D, Department of Radiology, University of Connecticut Health Center, Farmington, CT 06032, USA (Tel 203-674 3322)

HPA Annual General Meeting and IPSM Scientific Meeting
September 15–19, 1987
Liverpool
Further details IPSM, 47 Belgrave Square, London SW1X 8QX (Tel 01-235 6111).

6th International Workshop on Bone and Soft Tissue Densitometry
September 22–25, 1987
Palace Hotel, Buxton, Derbyshire
Further details: Dr J E Adams, Senior Lecturer, Department of Diagnostic Radiology, Stopford Building, Oxford Road, Manchester M13 9PT

Basic Review and Current Concepts in Neuroradiology and Head and Neck Radiology
October 12–16, 1987
Boston, Massachusetts, USA
Further details. Harvard Medical School, Department of Continuing Education, Boston, MA 02115, USA (Tel 617-732 1525)

RCR Interventional Radiology Course
October 13–15, 1987
Hotel St George, Sheffield
Further details. Dr D C Cumberland, Consultant Radiologist, Northern General Hospital, Sheffield S5 7AU (Tel. 0742-434 343 ext 4828).

RADIOLOGIST

Radiologist wanted with minimum experience of five years in CT Scan. The terms are on percentage basis and negotiable. This job is preferable for those candidates who are from Bombay and who want to return to India for permanent settlement.

Please apply with full bio-data and three references to:

THE MEDICAL DIRECTOR
CUMBALLA HILL HOSPITAL,
95, AUGUST KRANTI MARG,
BOMBAY 400 036. INDIA.

DIAGNOSTIC RADIOLOGIST

A diagnostic radiologist, of at least senior registrar level, to serve one year in visiting professor status in Department of Radiology at Texas Tech University School of Medicine.

Will do general diagnostic radiology including angiography and interventional procedures.

Please send cv and three letters of reference to:

Jay P Sackler, Chairman of Radiology,
Texas Tech University School of Medicine,
Lubbock, Texas 79413.

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All enquiries for advertising space should be addressed to:

Advertisement Dept, The British Journal of Radiology, 36 Portland Place, London W1N 4AT. Tel.: 01-631 1168, 01-580 4085

NEURORADIOLOGIST

Department of Radiological Sciences, Ottawa Civic Hospital, a 932 bed teaching hospital, is looking for a neuroradiologist commencing April 1987 Group consists of 13 radiologists and remuneration is fee for service.

Contact Dr G Belanger, Chief, Department of Radiological Sciences, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, Canada K1Y 4E9 Telephone 613-725-4982.

ULTRASOUND UPDATE
Wednesday 18 March 1987
HILLINGDON HOSPITAL

Course Organiser: Dr Diz Shirley

This study day has been specially designed to be of interest to radiologists, radiographers, paediatricians and obstetricians.

Leading experts in state of the art ultrasound will discuss the following topics.

PAEDIATRIC CARDIAC ULTRASOUND
NEONATAL INTRACRANIAL ULTRASOUND
GENERAL PAEDIATRIC ULTRASOUND
PRE-NATAL ECHOCARDIOGRAPHY
ULTRASOUND DIAGNOSIS OF FOETAL ANOMALIES
INTERVENTIONAL ANTENATAL ULTRASOUND
SAFETY OF DIAGNOSTIC ULTRASOUND MACHINES
GENERAL INTERVENTIONAL ULTRASOUND

Application has been made for approval for study leave under HM(67)27.

Course Fee: £25 (to include lunch).

For a detailed programme and application form apply to the Postgraduate Administrator, Hillingdon Hospital, Uxbridge, Middx UB8 3NN. Tel: 0895 37964/38282 Ext. 253.

The British Institute of Radiology Nycomed Scandinavian Scholarships
1988

The British Institute of Radiology invites applications for the 1988 Nycomed Scandinavian Scholarships.

These Scholarships, which are generously funded by Nycomed (UK) Ltd, enable United Kingdom diagnostic radiologists, preferably members of the British Institute of Radiology, to visit Scandinavian academic departments for up to two months' concentrated study, free of financial constraints: a maximum of £2500 per month will be provided.

The purpose of the Nycomed Scandinavian Scholarships is to enable diagnostic radiologists of senior registrar or junior consultant status, interested in diagnostic or interventional procedures concerned with intravascular contrast media, to visit one or more academic departments of radiology in Scandinavia (Norway, Sweden, Denmark) for in-depth radiological experience of up to two months. Each recipient will be responsible for his/her itinerary, travel, accommodation and insurance arrangements, subject to the approval of the BIR.

A condition of each scholarship is that a report of work undertaken, in a form suitable for publication in the Bulletin of the British Institute of Radiology, shall be submitted.

Applications for 1988 should be submitted by **31 July 1987** and interviews will take place in September.

Nyegaard (UK) Limited wishes to announce there has been a change of Company name to : NYCOMED (UK) LIMITED.

For further information please write to:
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THE BRITISH JOURNAL OF RADIOLOGY

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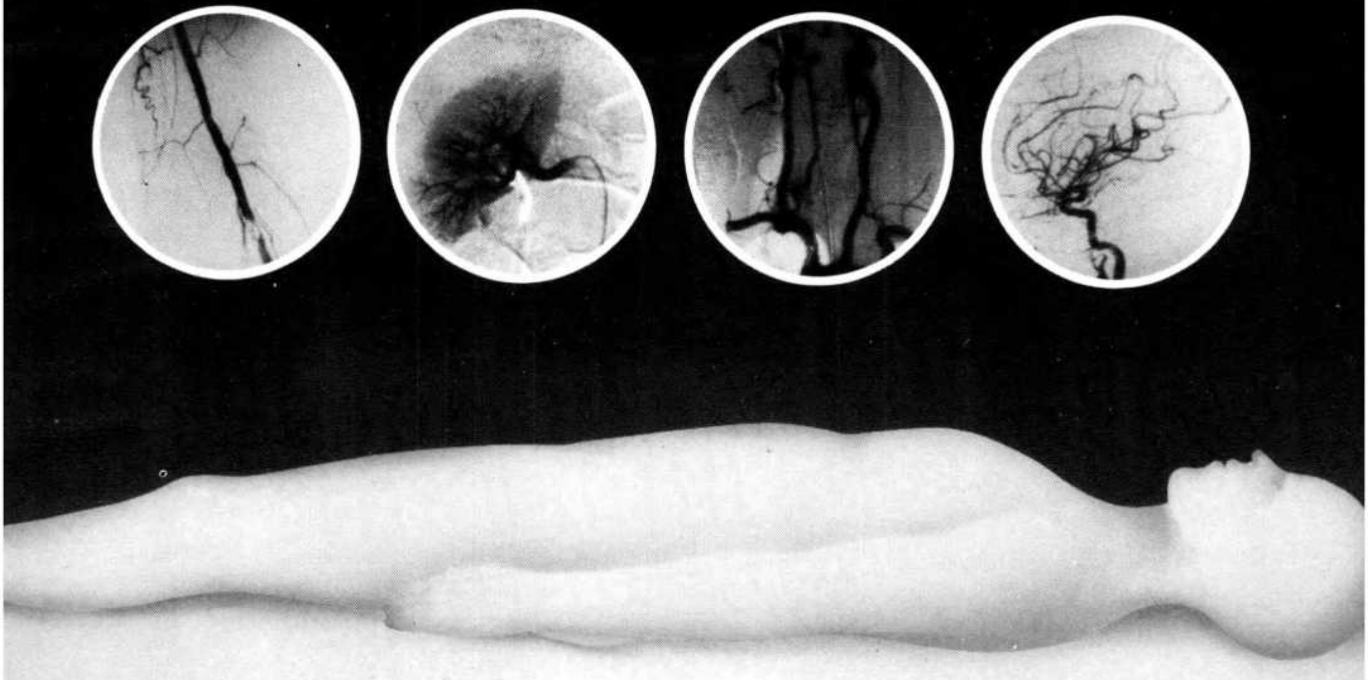

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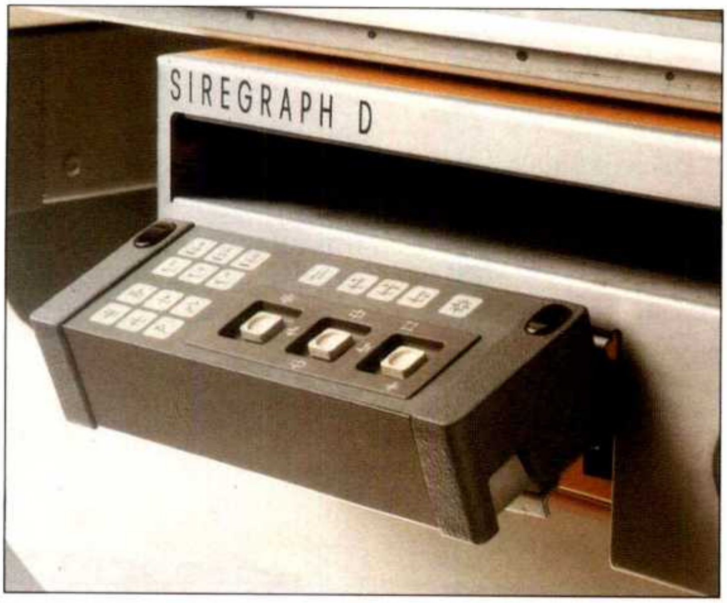

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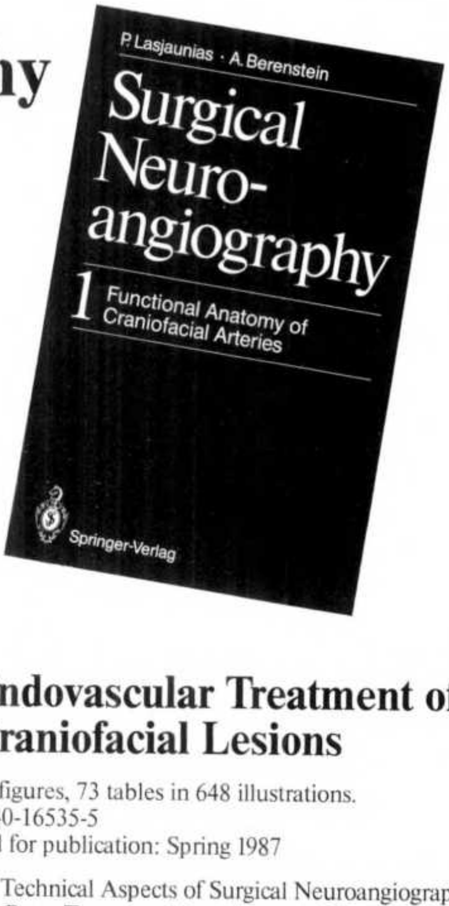
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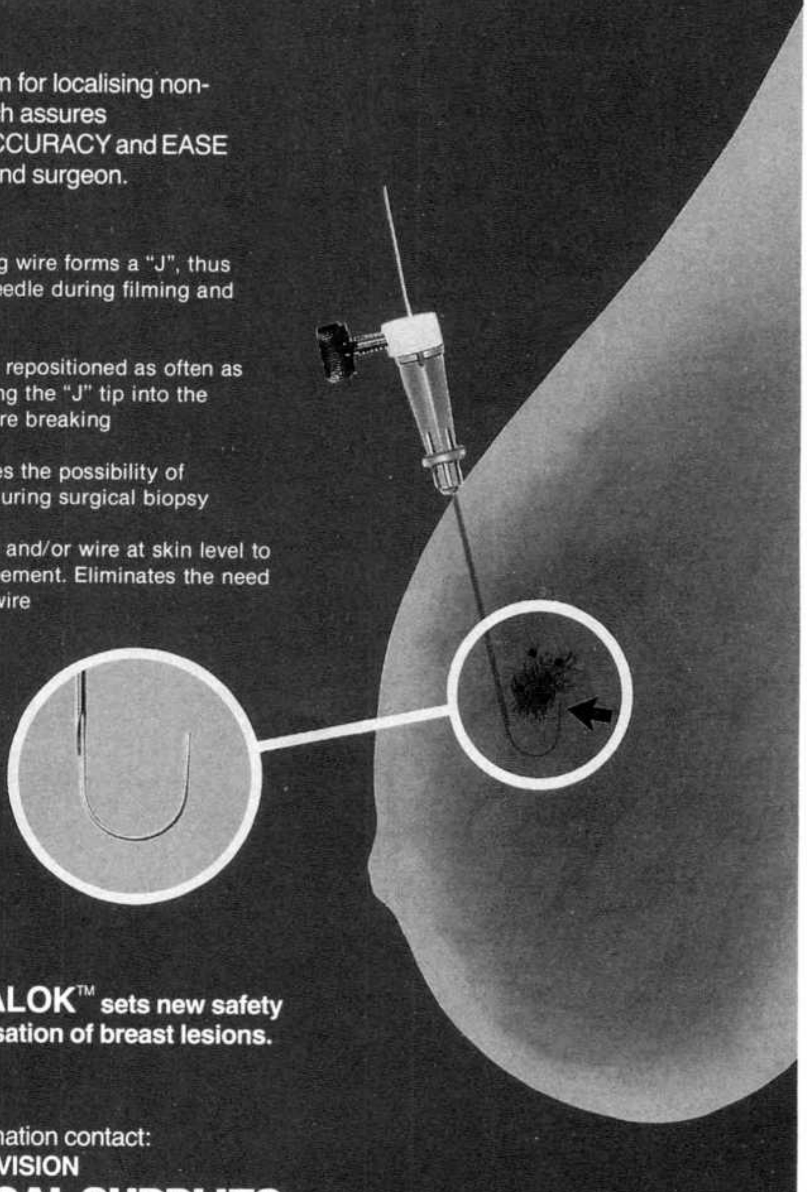

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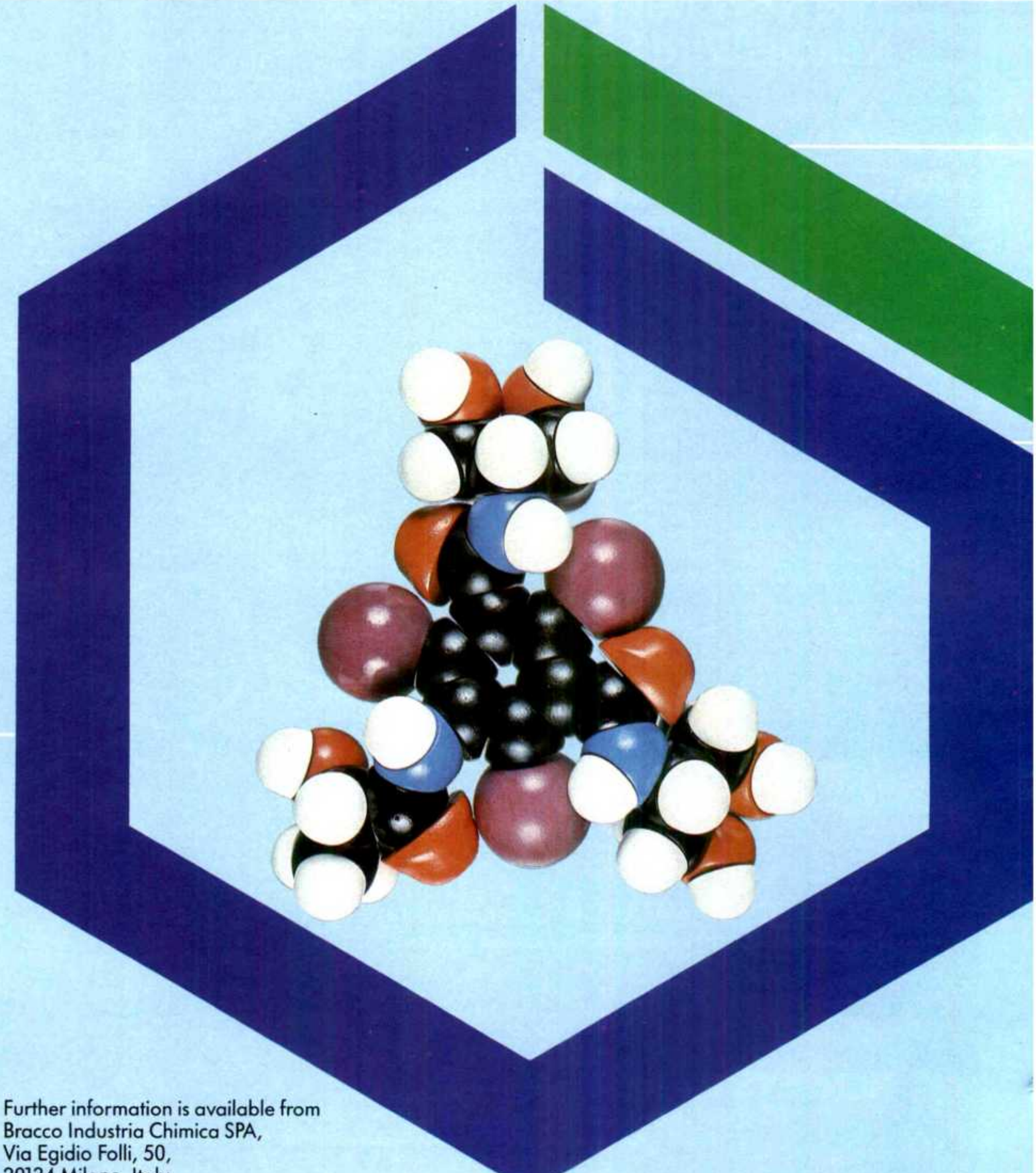

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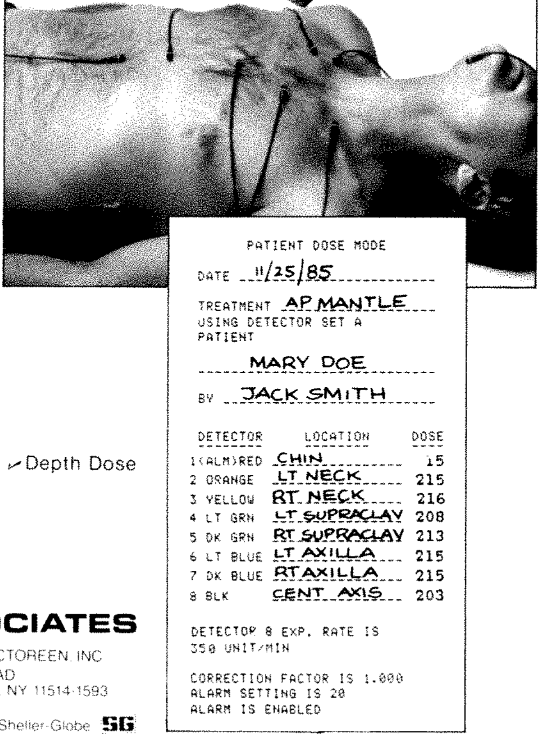

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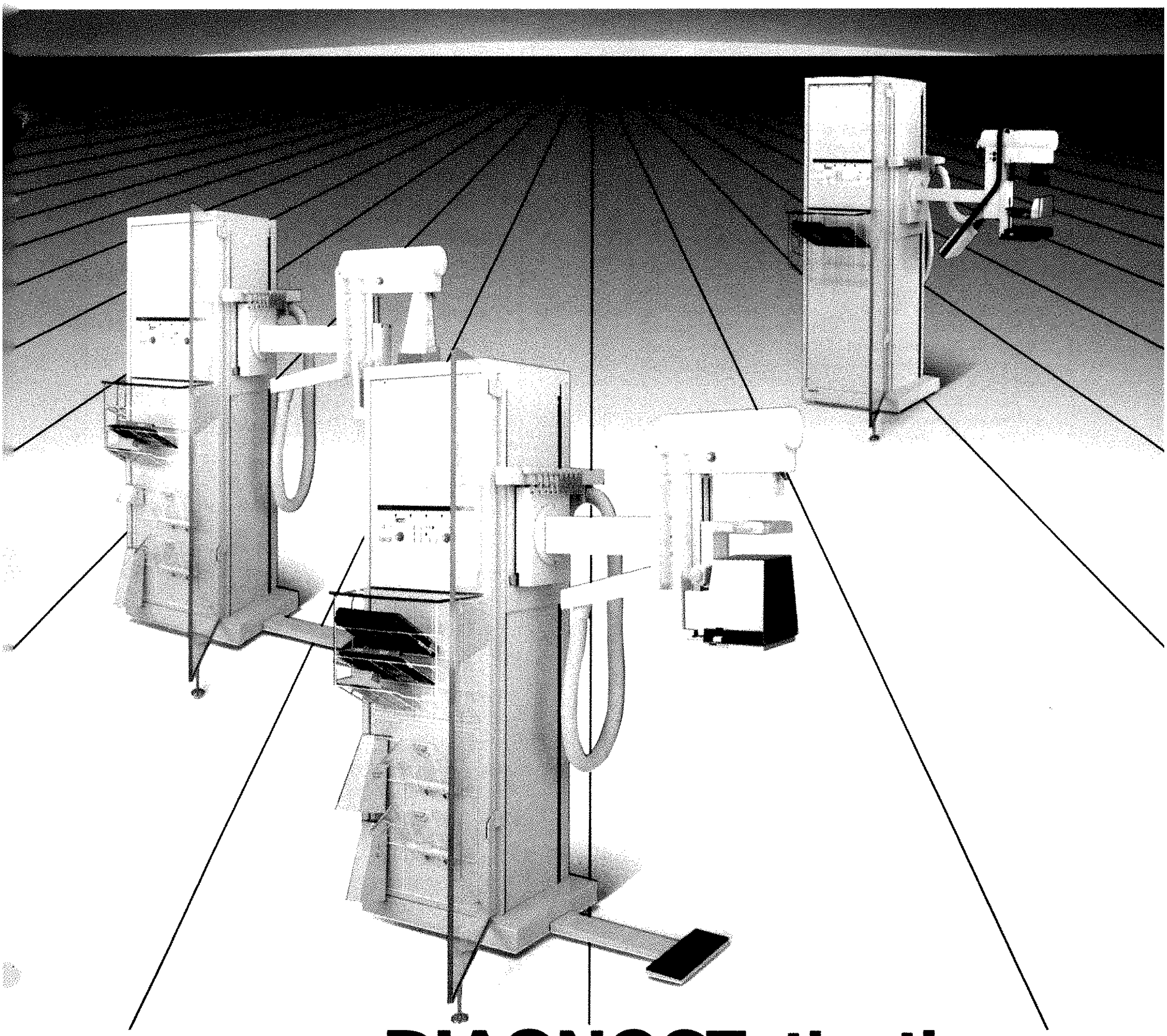

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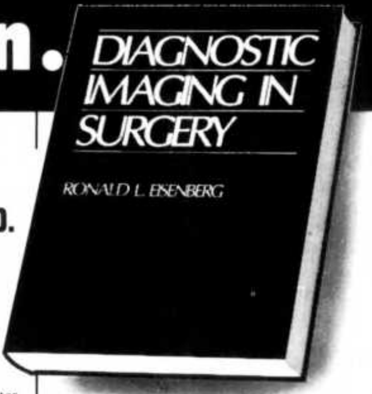

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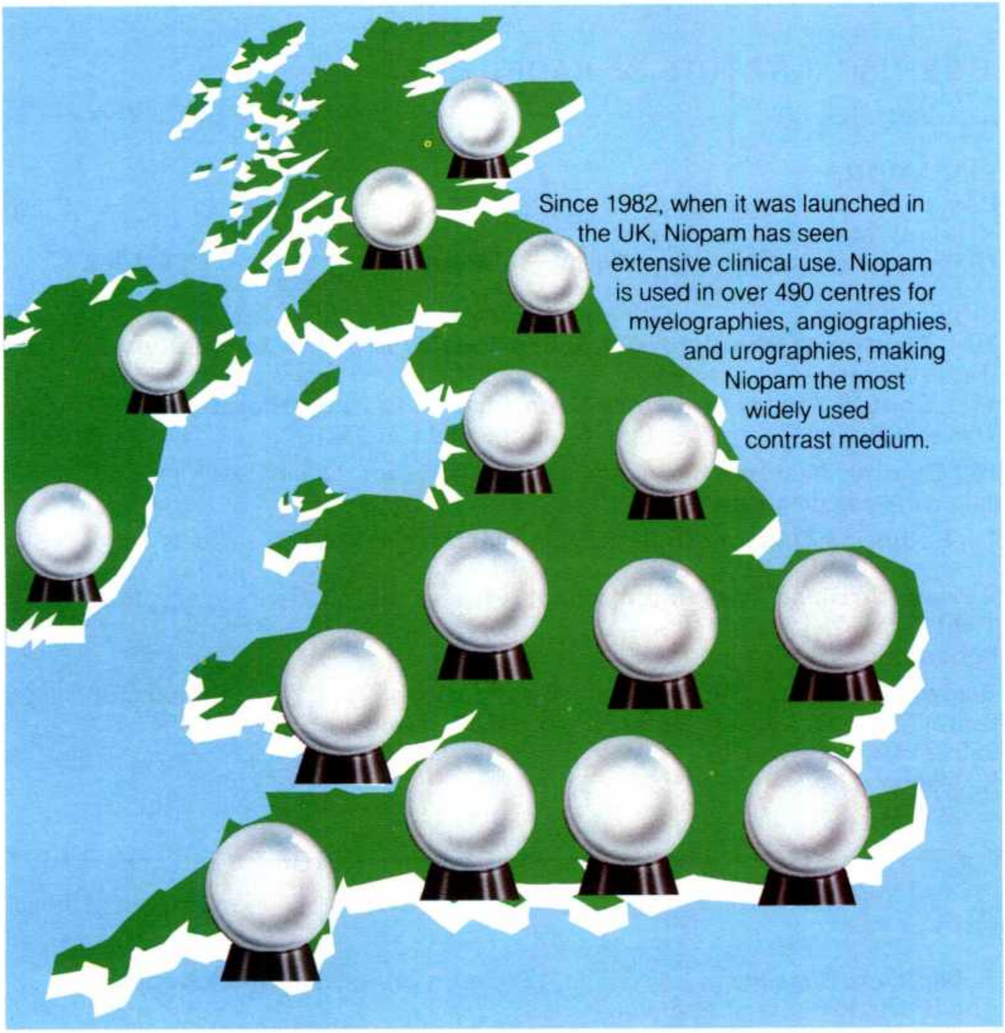
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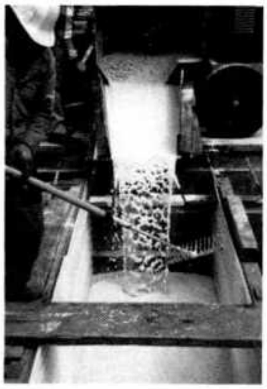

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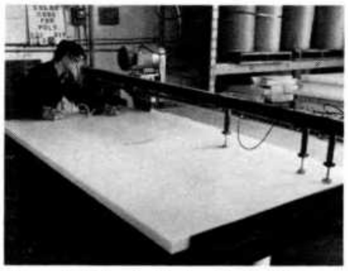

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Measurements of internal auditory meatus by polytomography. 1. Normal subjects

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(*Received January 1986 and in revised form June 1986*)

ABSTRACT

Polytomography permits clear visualisation of the internal auditory meatus (IAM), the normal range of measurements of which is important for radiograph interpretation. Previous reports indicate wide variation in vertical diameter and in the length of the posterior canal wall although in any one individual there is usually little variation between the two sides. We studied the relationship of both the vertical diameter and the length of the posterior walls of the IAM to the growth of the skull and pneumatisation of the temporal bone in 300 patients with no evidence of a lesion of the VIII nerve. No statistically significant correlation was observed between these factors.

While polytomography permits clear visualisation of the internal auditory meatus (IAM), knowledge of the normal range of measurements is also important for radiograph interpretation. Measurement of the normal meatus by polytomography has already been reported by Sato and Takida (1962) and Valvassori and Piece (1964), who show that the individual differences in the vertical diameters and the posterior wall lengths are large, but there is little variation between the two sides in the same individual. We have studied how the vertical diameter and posterior wall length of the IAM are related to the growth of the skull and pneumatisation of temporal bone.

SUBJECTS

The subjects in this study were 180 men and 120 women, age range 15–77 years (average 47.9, SD 13.8 years) who visited the Outpatient Clinic, Department of Otorhinolaryngology, Kanto Rosai Hospital. Cases with tumours involving the VIII nerve were excluded.

METHODS

Measurement of internal auditory meatus

Six radiographs were taken in coronal section at intervals of 2.5 mm using a camera (LT—UA, Hitachi) for tomography Of these radiographs, those in which the IAM was shown most clearly were used to measure the maximum vertical diameter and posterior wall length (Fig. 1). The magnifying power of this camera is 1 30, but correction of the measurements was not made.

Shape of internal auditory meatus

The IAMs were divided into three morphological types using the classification of Kodera and Iinuma (1974) (Fig. 2).

Measurement of skull

The distance between the cochleas was used as an index of skull size and this was measured on those tomograms in which the cochleas were most clearly shown (Fig. 3).

Measurement of development of pneumatisation of the temporal bone

Development of pneumatisation on the plain radiographs made in the Sonnenkarb projection was measured by the rectangular method (Imai et al, 1978) (Fig. 3).

RESULTS

Shape of the internal auditory meatus

The IAMs were classified morphologically as: cylinder type, 436 ears (72.7%), bud type, 137 ears (22.8%), and funnel type, 27 ears (4.5%). Differences in shape on the right and left sides were found in 33 cases (11.0%).

Vertical diameter

The vertical diameter ranged between 12.0 mm and 3.5 mm, average 6.8 mm (SD 1.28 mm); there was

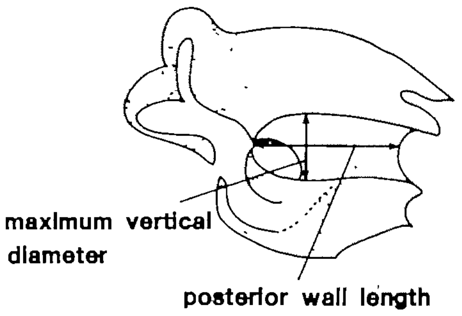

FIG 1

Measurements of the IAM.

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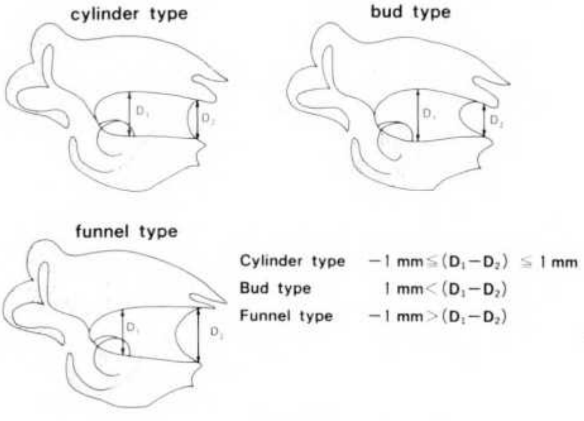
cylinder type
bud type
funnel type
D₁
D₂
Cylinder type −1 mm ≦ (D₁−D₂) ≦ 1 mm
Bud type 1 mm < (D₁−D₂)
Funnel type −1 mm > (D₁−D₂)

FIG. 2.

Morphological classification of the IAM.

considerable individual variation. Comparison between sexes showed the meatus to be significantly larger in males ($p < 0.0001$) (Fig. 4).

Maximum variation between sides in the same individual was 3.0 mm; the average variation was 0.47 mm (SD 0.50 mm). In 286 subjects (95.3%) the variation between sides was less than 1.0 mm (Fig. 5).

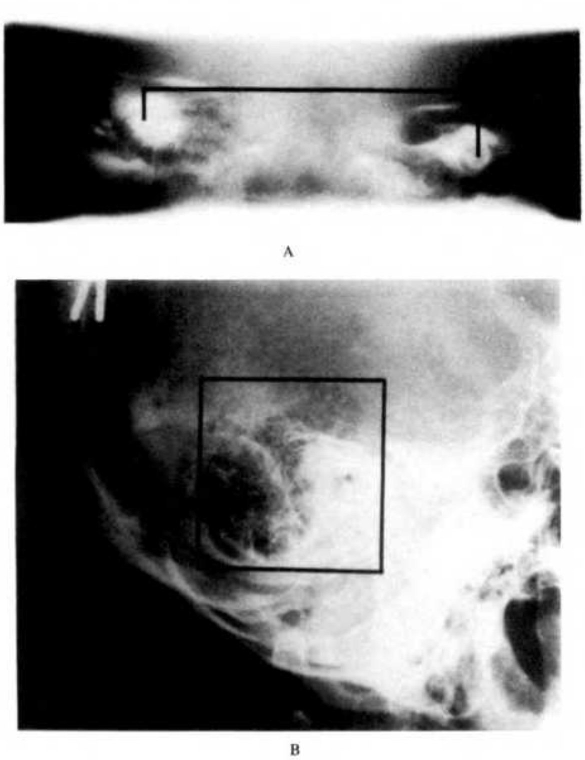

FIG. 3.

(A) Distance between right and left cochleas and (B) area of pneumatisation of temporal bone.

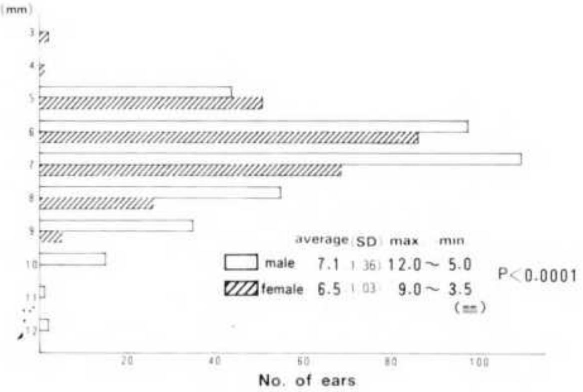

FIG. 4.

Distribution of the maximum vertical diameter of the IAM.

Posterior wall length

The posterior wall length was 18.0 mm maximum, 4.0 mm minimum, average 8.7 mm (SD 2.30 mm). There was considerable difference between individuals (Fig. 6) and variation between sides was 4.0 mm maximum, averaging 0.85 mm (SD 0.79 mm). Differences between sexes were, again, significant ($p < 0.001$) (Fig. 7).

Distance between cochleas

The distance between cochleas was 10.4 cm maximum, 7.7 cm minimum, average 9.0 cm (SD 4.79 cm) (Fig. 8). Differences between the sexes were significant ($p < 0.0001$).

Development of pneumatisation of temporal bone

This was 48.3 cm^2 maximum, 0.7 cm^2 minimum, average 20.1 cm^2 (SD 8.80 cm^2) (Fig. 9). The difference in area between sides in each individual averaged 5.1 cm^2 in men and 4.5 cm^2 in women.

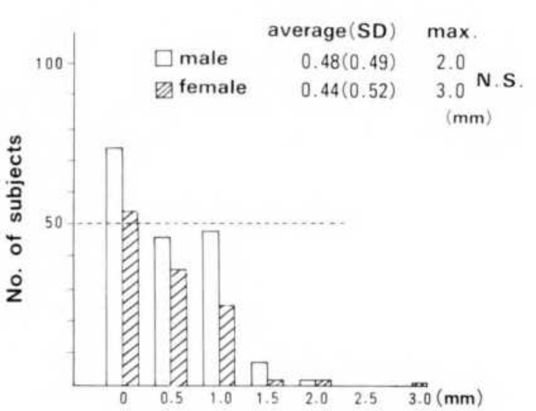

FIG. 5.

Distribution of the variation between sides in the same individual in the maximum vertical diameter of the IAM.

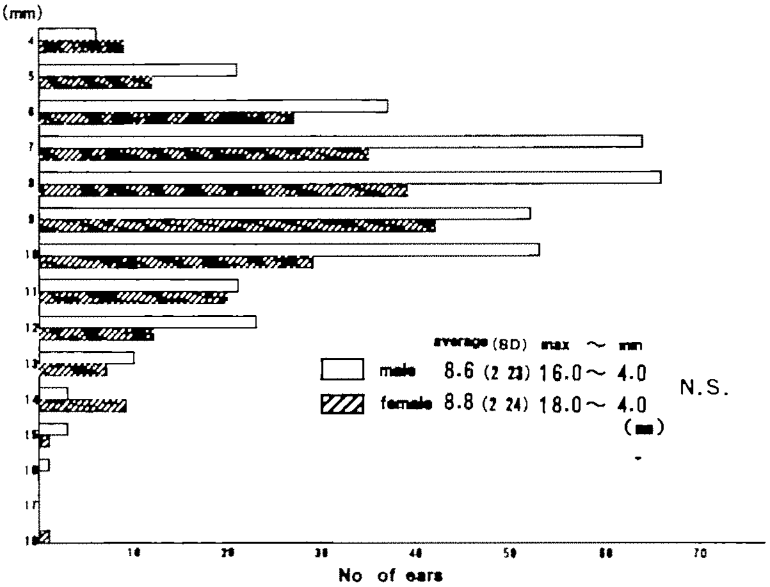

FIG. 6.

Distribution of the posterior wall length of the IAM.

Correlation of results

The results of measurement of the maximum vertical diameter, posterior wall length, distance between cochleas and development of pneumatisation were studied by regression analysis and are presented in Table I. No statistically definite correlation was observed.

DISCUSSION

Shape

Morphological classifications of the IAM have been made by Camp and Cilley (1939), Valvassori and Piece (1964), Amjad et al (1969), Papangelou (1972) and Kodera and Iinuma (1974).

Camp and Cilley (1939) reported the IAMs to be cylindrical in type in 60%, narrowed medially in 16%, oval in 12% and narrowed laterally in 12%. Valvassori and Piece (1964) found the meatuses to be cylindrical in 51%, narrowed medially in 30%, oval in 19% and narrowed laterally in 0%. The difference between the observers is accounted for by differences in morphological classification.

Kodera and Iinuma (1974) reported cylindrical type in 61.5% and bud type in 38.5% using a postero-anterior projection, and cylindrical type in 54.8%, bud type in 45.2% and funnel type in 0% using Stenver's projection.

Our measurements showed the cylindrical type in 72.7%, slightly higher than the figures found by other observers, and the funnel type in 4.5%.

Variation in shape between sides in an individual was found in 30% by Camp and Cilley (1939), 10% by Valvassori and Piece (1964) and 11% in this study.

Table II presents the values of our IAM measurements.

For direct measurement of the IAM, methods such as silicone moulding, histological tomography and radiography of temporal bone are employed. For indirect measurement, methods such as postero-anterior projection, Stenver's projection, tomography and polytomography are available.

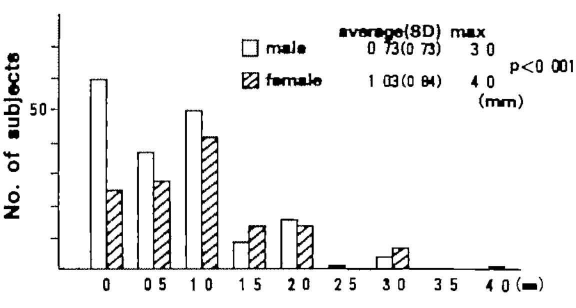

FIG 7

Distribution of variation between sides in the posterior wall length

Vertical diameter

The maximum vertical diameter of the IAM by direct measurement was within the range 2.0–11 mm, averaging about 5 mm. Using indirect measurement with antero-posterior radiographs, the range was similar, 2.0–12 mm.

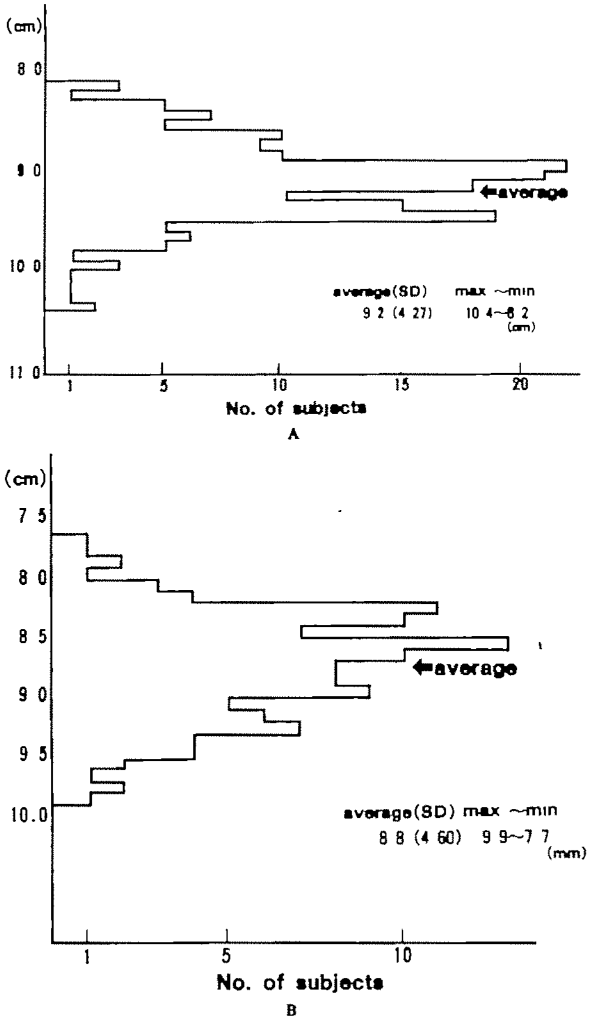

FIG. 8.

Distribution of the distance between the cochleas: (A) men and (B) women

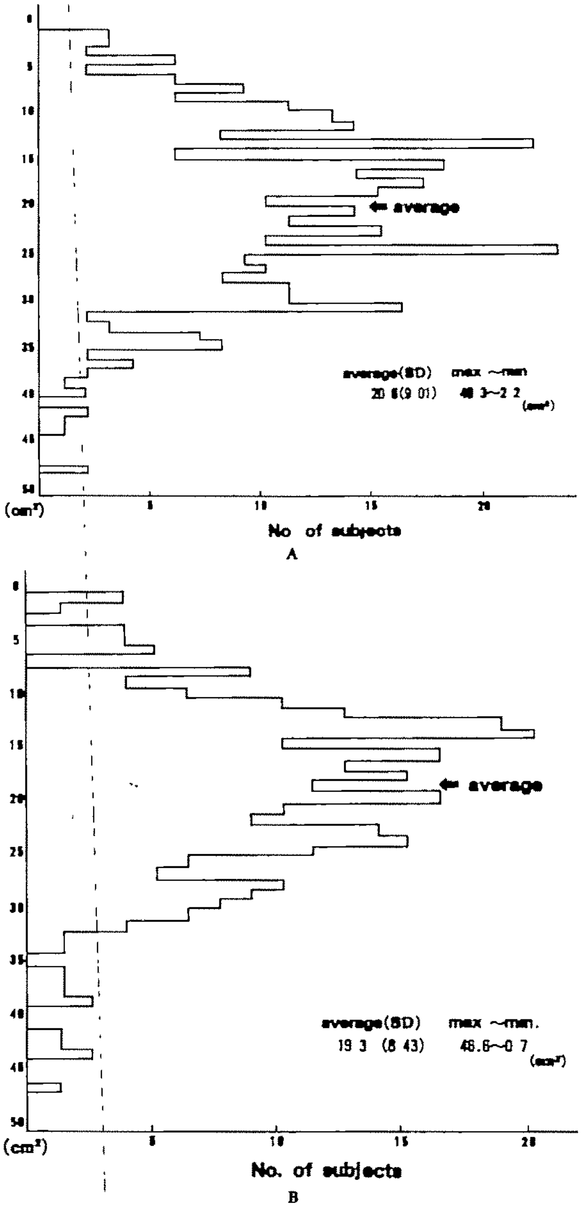

FIG. 9

Distribution of the development of pneumatisation of temporal bone: (A) men and (B) women.

Valvassori and Piece (1964) used polytomography as in this series; their values were 2.0–8.0 mm (average 4.0 mm), which are slightly less than our measurements.

Previous investigators have found variation between sides in the vertical diameter to be 2.0 mm or less in

TABLE I

CORRELATION OF THE PARAMETERS

	Correlation coefficients and regression-line equations, respectively		
	Vertical diameter	Posterior wall length	Distance between cochleas
Posterior wall length	−0 10 $Y = -0.16X+9\ 79$		
Distance between cochleas	0.14 $Y = 0.05X+8.65$	0 08 $Y = 0.02X+8\ 86$	
Area of pneumatisation of temporal bone	0.10 $Y = 0.67X+15.45$	0 15 $Y = 0.57X+15\ 17$	0.05 $Y = 0.00003X+8.95$

TABLE II

RESULTS OF PREVIOUSLY REPORTED MEASUREMENTS OF THE INTERNAL AUDITORY MEATUS

	Ebenius, 1934	Camp & Cilley, 1939	Graf, 1952	Sato & Takida, 1962	Valvassori & Piece, 1964	Yanagihara et al, 1967	Lapayowker, 1969	Papangelou, 1972	Kodera & Iinuma, 1974	This report
Vertical diameter (average) (mm)	5.0–9.0 (6.3)	2.5–11.0 (5.2)	3.0–6.5 (4.7)	1.4–3.7 (3.0)	2.0–8.0 (4.0)	3.5–7.7 (5.3)	3.0–10.5	2.0–7.0 (4.6)	4.0–8.0 (5.8)	3.5–12.0 (6.8)
Bilateral variation (%)										
<1 mm	96	75			99	100	100	87	96	95.3
1–2 mm	3	23			1			9	4	4.3
2–3 mm	1	2			0			4	0	0.3
Posterior wall length (average) (mm)		3.0–16.0 (7.8)	5.0–11.0 (8.0)	5.1–10.2 (7.1)	4.0–11.0 (8.0)	6.0–12.0 (7.9)		6.0–14.0 (9.2)	4.0–11.0 (7.2)	4.0–18.0 (8.7)
Bilateral variation (%)										
<1 mm		27			86			59	71	78.4
1–2 mm		38			13			35	27	18.4
2–3 mm		23			1			6	2	4.0
>3 mm		12			0			0	0	0.2
No. of subjects	200 (100 pairs)	509 (including 250 pairs)	60	60 (30 pairs)	300 (including 100 pairs)	38 (19 pairs)	100 (50 pairs)	242 (121 pairs)	400 (200 pairs)	600 (300 pairs)
Method	30° fronto-occipital (Towne) projection	AP projection	Histological	Polytomography	Polytomography	Tomography	Tomography	Cast	PA projection	Polytomography
Magnifying power	1.28	1.0	1.0	1.0	1.0 (corrected)	1.1	unknown	1.0	1.15	1.30

96–100% of cases and this was confirmed in our series, so that although the normal range of the maximum vertical diameter of the IAM is extensive, where the variation between left and right side exceeds 2.0 mm, it should be considered pathological.

Posterior wall length

The length of the posterior wall was within the range 3.0–16.0 mm by direct measurement and within the range 4.0–18.0 mm by indirect measurement. The value reported by Valvassori and Piece (1964) was 4.0–11.0 mm, a slightly smaller range than in our series.

Difference in length of the posterior walls in an individual was not more than 3.0 mm in any reported series except that of Camp and Cilley (1939).

Finally, correlation of the vertical diameter and posterior wall length with the growth of the skull or the development of pneumatisation of the temporal bone showed no relationship of statistical significance. There was a tendency for the posterior wall length to become shorter as the vertical diameter increased, with the coefficient of correlation being -0.10 and equation of regression line $y = -0.16 \times +9.79$. Since the posterior wall length is measured almost in the centre of the posterior wall, as illustrated in Fig. 1, the innermost part of the meatus becomes an arc as the vertical diameter becomes larger, presumably accounting for the shortening of the posterior wall. It would be reasonable to expect a relationship between the vertical diameter and posterior wall length on the one hand and growth of the skull on the other, but this was not so in this study, perhaps because the distance between the cochleas was the only parameter used as an index of skull growth. However, it can be firmly stated that there is no correlation between the growth of the IAM and the degree of pneumatisation of the temporal bone.

Acknowledgments

We thank Professor Michinari Okamoto, M.D., Department of Otolaryngology, School of Medicine, Showa University, Tokyo, Japan.

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Computed tomography of the post-operative lumbar spine: the need for, and optimal dose of, intravenous contrast medium

By A. K. Dixon, M.A., M.R.C.P., F.R.C.R. and *R. P. Bannon, M.B., B.S., F.R.C.R.
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(*Received May 1986 and in revised form September 1986*)

ABSTRACT

Forty-five patients who had undergone previous lumbar spine surgery with symptoms and signs warranting further investigation were examined by computed tomography (CT). The findings in three separate subgroups of 15 patients were compared. The first randomly selected group underwent CT without the use of intravenous contrast medium; the second and third groups were examined both before and after the administration of contrast medium, using 16.25 g and 32.5 g iodine, respectively. In the latter two groups the CT studies were reported both before and after enhancement. In the 15 patients in the first group (no contrast medium), uncertainty as to whether disc material or fibrosis was responsible for the radiological abnormalities was expressed in the final report at six of the 20 post-surgical sites. Among the 30 patients who received contrast medium, 40 post-surgical sites were examined, at six of these sites there was no radiological cause for concern; at 16 sites there were unequivocal radiological appearances of either disc material or fibrosis. Enhancement resolved the radiological uncertainty at 13 of the remaining 18 sites, almost always by reinforcing the initial radiological opinion; this left five sites where uncertainty persisted in the final report. The larger dose of contrast medium caused the more marked enhancement of those abnormalities considered to be due to fibrosis, although enhancement was readily recognised using the lower dose. While intravenous enhancement assists radiological interpretation at those sites where diagnostic uncertainty persists after routine CT, it would seem that it is not essential in patients in whom routine CT studies show no serious abnormality or the characteristic appearances of disc material or fibrosis.

Surgery is a far from certain cure for lumbar spine lesions (Burton et al, 1981); continuing, recurrent or new signs and symptoms are all too common. Both radiculography (Quencer et al, 1977) and computed tomography (CT) (Teplick & Haskin, 1983) may be difficult to interpret following surgery as both disc material and post-operative fibrosis can cause similar radiographic signs. But now that many of the appearances on CT following surgery are better recognised (Teplick & Haskin, 1983), CT is emerging as the favoured test in these circumstances—particularly by the patient, who will usually have had previous experience of radiculography. However, differentiation between disc and fibrotic material remains a problem. Some advocate repeating CT after a time interval; the volume of fibrosis may shrink with time whereas disc fragments will remain static or even increase in size with further herniation.

Schubiger and Valavanis (1982) were the first to report the enhancing effect of intravenous contrast medium on scar tissue, thus allowing differentiation from disc material. Since then, this technique has been used in many centres with varying enthusiasm (Chafetz et al, 1983; Teplick & Haskin, 1984). However, Braun and colleagues (1985) have recently confirmed that enhancement increases the level of confidence and diagnostic accuracy when attempting to differentiate disc material from scar tissue. Because repeated cuts and the administration of contrast medium add to the time, expense, radiation dose and risk of the procedure, we have assessed also the effect of intravenous contrast medium. In particular, we have assessed how often enhancement changes the radiological opinion and how two different doses of contrast medium alter the degree of enhancement.

PATIENTS AND METHODS

Forty-five patients referred for CT because of continuing, recurrent or new clinical symptoms following previous lumbar spine surgery were prospectively studied. Initially, 30 consecutive patients were randomly divided into two groups. One group (Group A) of 15 patients underwent CT of the lumbar spine without the use of intravenous contrast medium; this forms a control group. The second group (Group B) also had an initial routine CT study but, in addition, those anatomical sites within the field of previous surgery which appeared abnormal were re-examined during the 2–3 min immediately following an intravenous injection of 50 ml sodium/meglumine diatrizoate (Urografin, Schering) (325 mg I/ml) given over approximately 2 min. At the end of this initial study it transpired that the dose of contrast medium was less than that used in other centres. Accordingly, 15 further patients (Group C) were examined before and after injection of contrast medium, this time giving 100 ml of urographic contrast medium over approximately 3 min. The contrast medium used was usually diatrizoate (Urografin) but a

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non-ionic contrast medium, iopamidol (Niopam, Bracco; 300 mg I/ml), was used where there were appropriate indications (*e.g.* mild asthma).

Our CT routine for the examination of the lumbar spine has been developed over 4 years and is generally similar to that used elsewhere. It employs 4 mm-thick cuts and 5 mm increments. For each disc space, cuts extend from the pedicles of one vertebra to the pedicles of the next. Intervening cuts to obtain perfect delineation of the disc or other additional cuts are obtained as required (Dixon, 1983).

In each patient, any abnormality within the previous operative field was noted. Particular attention was paid to abnormal tissue impinging on the theca or nerve roots. Only a small proportion of the abnormalities included for further analysis were considered, on radiological grounds, to be surgically significant. Furthermore, in several patients, radiological abnormalities were demonstrated at levels outside the previous surgical field and these are not considered further in this study.

At each abnormal site the attenuation value of the abnormal tissues was measured (HU) by using a region-of-interest facility on the independent console. Inevitably, for small lesions, difficulties arose from partial volume effects of adjacent bone or fat and on occasions this measurement was impossible.

A subjective assessment was made as to whether the signs were more suggestive either of residual disc material or fibrosis in its various forms. This assessment was made in the light of the known appearances on CT of disc material and fibrosis (Teplick & Haskin, 1983) and depended mainly on the site and shape of any abnormal soft tissue, its relation to the thecal sac and disc space, any alterations to the fat planes around the theca and the density of the lesion itself. Seven subjective assessments were used ranging from definite fibrosis (F) to definite disc material (D) (Table I). In those patients receiving contrast medium (Groups B and C) the radiological assessments and attenuation measurements were made both before and after enhancement (giving both an initial and a final assessment).

RESULTS

Among the total of 45 patients studied, there were 60 levels at which there was CT evidence of previous surgery; at 12 of these sites there was no abnormality which could have been confused with disc material or fibrosis and these sites will not be considered further (Fig. 1). Six of these sites were in Group A (no contrast medium), two in Group B (50 ml contrast medium) and four in Group C (100 ml contrast medium). Accordingly, there were 48 sites with abnormalities of varying character and significance available for detailed evaluation. Fourteen of these sites were in Group A, 17 in Group B and 17 in Group C.

The radiological assessments of the abnormal sites are shown in Fig. 2. For Groups B and C both pre- and post-contrast assessments are given. It can be seen that at initial assessment 24 abnormalities were considered to be definitely due to either fibrosis (nine) or disc residua (15). In the 16 of these definite abnormalities which were in Groups B and C there was no change in the radiological assessment following enhancement. Uncertainty as to the nature of the abnormality at the initial assessment existed at 24 sites (six of these in Group A). In the 18 sites in Groups B and C where there was uncertainty on the initial assessment, enhancement resolved the radiological uncertainty at 13 sites, leaving five sites with less than definite assessment (three in Group B, two in Group C). In 10 of the 13

TABLE I

THE CLASSIFICATION OF RADIOLOGICAL OPINION

F	Definite fibrosis
F ≫ D	Fibrosis much more likely than disc
F > D	Fibrosis more likely than disc
E	Equivocal interpretation
D > F	Disc more likely than fibrosis
D ≫ F	Disc much more likely than fibrosis
D	Definite disc

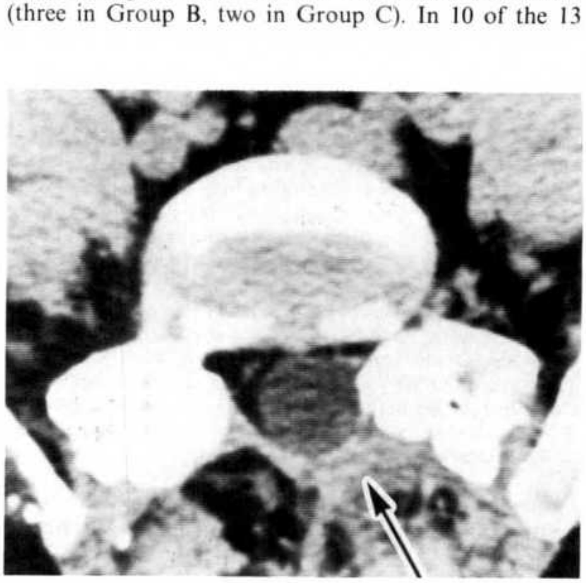


FIG. 1.

A CT cut through the L5–S1 disc in a 53-year-old male in Group B. Note the considerable thickening of the tissue planes adjacent to the left posterior aspect of capacious thecal sac due to previous surgery (arrow). There is excellent delineation of the disc and the anterior aspect of theca by epidural fat. The epidural vessels can just be identified and that on the right is completely surrounded by epidural fat. The epidural vein on the left is less well seen, due to the theca being pulled to the left by the left posterolateral fibrosis. No evidence is visible of significant disc fragment or fibrosis anterolateral to the theca. Enhancement here merely made the epidural veins slightly more obvious. The results from this site and 11 others with similar appearances were not considered further.

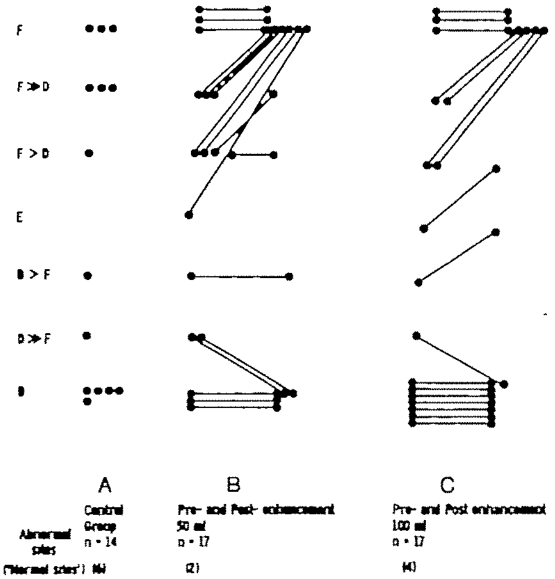


FIG. 2.

A chart showing the subjective radiological assessments in the three groups and the effect of enhancement.

sites the degree of change in confidence caused by enhancement was of one grade only (*e.g.* F ≫ D to F).

The relationship of attenuation values of the lesions to the radiological assessments are shown in Table II. In the control group (A) lesions considered to be due to fibrosis (F) had a mean value of 28 HU, while those likely to be due to disc (D) had a mean value of 65 HU. In the enhanced groups (B and C) the mean values of those abnormalities classed as F on the initial assessment were 40 HU and 32 HU, respectively, before enhancement and these values increased by 16 HU and 23 HU,

TABLE II

MEAN VALUES OF ATTENUATION MEASUREMENTS OF ABNORMALITIES ASSESSED. CORRELATION WITH RADIOLOGICAL OPINIONS. AT TWO SITES MEASUREMENT OF ATTENUATION WAS NOT POSSIBLE (NP, SEE TEXT). STANDARD DEVIATIONS ARE GIVEN IN PARENTHESES FOR THOSE MEANS WHERE THREE OR MORE VALUES ARE AVAILABLE

TABLE IIa: CONTROL GROUP A

Radiological opinion	No. of abnormal sites	Mean of attenuation values (HU)
F	3 (1 NP)	28
F ≫ D	3	55 (6)
F > D	1	55
E	–	–
D > F	1	37
D ≫ F	1	95
D	5	65 (11)

TABLE IIb: ENHANCED GROUP B (50 ML CONTRAST MEDIUM)

Initial radiological opinion	No of abnormal sites	Mean of attenuation values before contrast medium (HU)	Mean of attenuation values after contrast medium (HU)
F	3	40 (6)	56 (10)
F ≫ D	3	41 (16)	49 (18)
F > D	4	33 (12)	40 (9)
E	1	27	40
D > F	1	NP	NP
D ≫ F	2	62	72
D	3	71 (33)	68 (27)

TABLE IIc: ENHANCED GROUP B (50 ML CONTRAST MEDIUM)

Final radiological opinion	No. of abnormal sites	Mean of attenuation values before contrast medium (HU)	Mean of attenuation values after contrast medium (HU)
F	9	37 (12)	49 (15)
F ≫ D	1	44	46
F > D	1	28	25
E	0	–	–
D > F	1	NP	NP
D ≫ F	0	–	–
D	5	67 (24)	70 (19)

TABLE IId: ENHANCED GROUP C (100 ML CONTRAST MEDIUM)

Initial radiological opinion	No of abnormal sites	Mean of attenuation values before contrast medium (HU)	Mean of attenuation values after contrast medium (HU)
F	3	32 (14)	55 (19)
F ≫ D	2	30	68
F > D	2	56	89
E	1	70	79
D > F	1	81	72
D ≫ F	1	69	78
D	7	81 (16)*	85 (16)*

TABLE IIe: ENHANCED GROUP C (100 ML CONTRAST MEDIUM)

Final radiological opinion	No of abnormal sites	Mean of attenuation values before contrast medium (HU)	Mean of attenuation values after contrast medium (HU)
F	7	38 (18)	68 (19)
F ≫ D	–	–	–
F > D	1	70	79
E	1	81	72
D > F	–	–	–
D ≫ F	–	–	–
D	8	79 (15)*	84 (15)*

*One abnormality, obviously heavily calcified at 300+ HU, excluded.

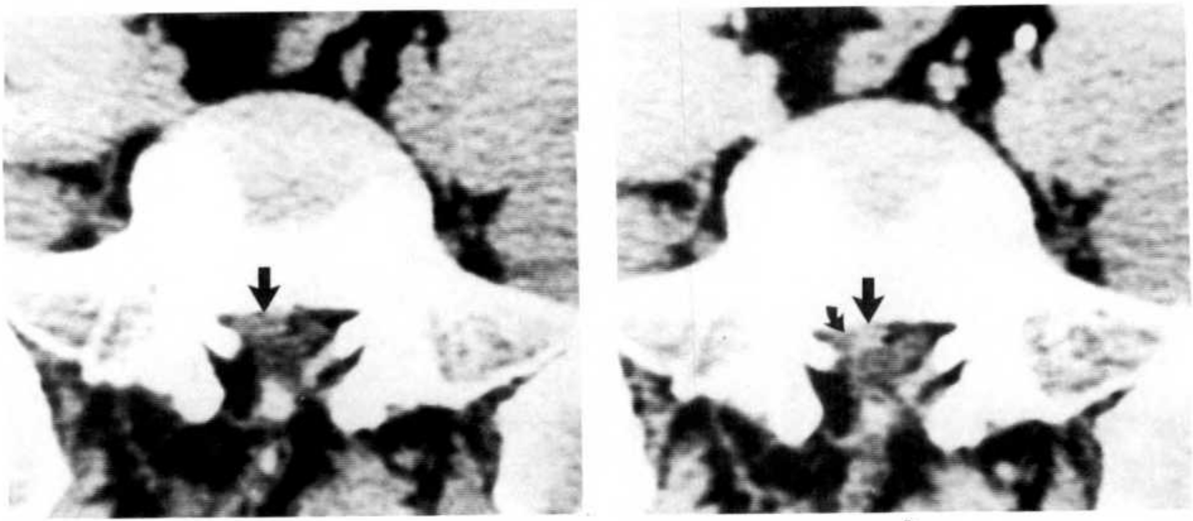


FIG. 3.

(A) A CT image just caudal to the L5–S1 disc in a 25-year-old man in Group B. The right S1 nerve root is obscured by a small area of abnormal soft-tissue-density material (27 HU, arrow). The right flaval ligament is absent due to previous surgery and there is little retraction of the sac. Initial radiological assessment was equivocal (E). (B) The same cut as in Fig. 3A following enhancement (50 ml contrast medium). Most of the abnormal material has enhanced (increasing to 40 HU, straight arrow). The right S1 root (unenhanced, small arrow) can just be identified laterally. So, too, can the unenhanced thecal sac posteriorly. Final radiological assessment: definite fibrosis (F). This example illustrates the most beneficial effect of enhancement seen in this series (E changing to F).

respectively, after use of contrast medium. Those abnormalities initially classed D measured 71 HU and 81 HU, respectively, and showed little change with contrast medium. Those lesions in the enhanced groups (B and C) finally assessed as F measured 37 HU and 38 HU before contrast medium and subsequently enhanced by 12 HU and 30 HU, respectively; those finally classed D measured 67 HU and 79 HU and, again, showed little change after contrast medium.

Illustrative examples are shown in Figs 3–8.

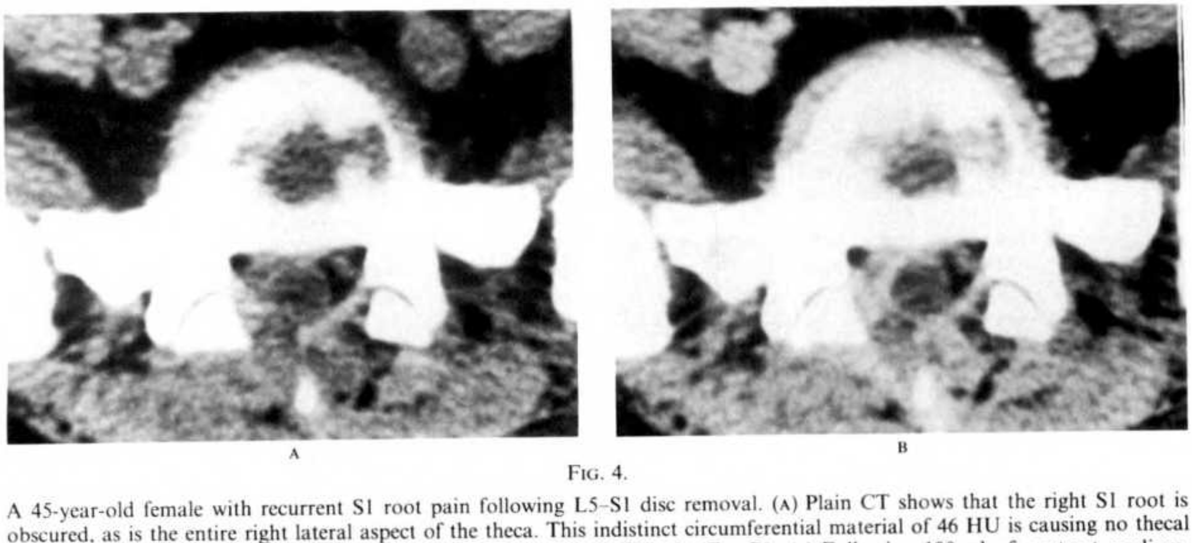


FIG. 4.

A 45-year-old female with recurrent S1 root pain following L5–S1 disc removal. (A) Plain CT shows that the right S1 root is obscured, as is the entire right lateral aspect of the theca. This indistinct circumferential material of 46 HU is causing no thecal displacement and was considered almost certainly to be due to fibrosis (F ≫ D). (B) Following 100 ml of contrast medium, enhancement (gain of +31 HU) is evident, leaving the thecal sac and S1 nerve root sheath unopacified. This was classified as definite fibrosis (F). The patient has been managed conservatively for presumed fibrosis.

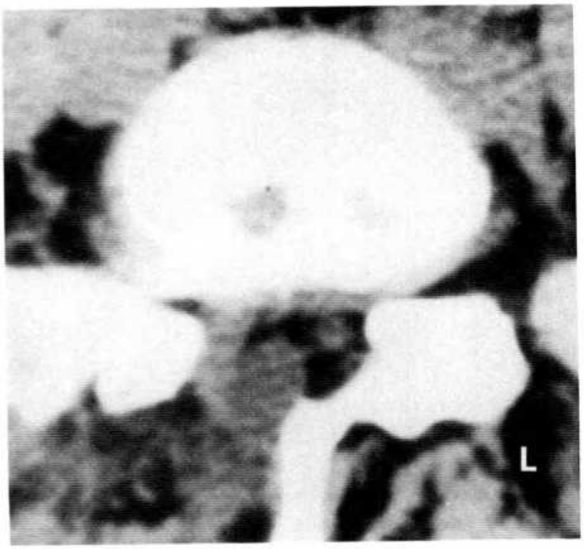


FIG. 5.

A 33-year-old male from Group A who had had right-sided L5–S1 disc surgery. The whole right lateral aspect of the theca is poorly defined and the sac is generally pulled towards the right, where it merges with a rind of soft tissue (33 HU). The right S1 root is presumably incorporated in this rind. The features were confidently interpreted as being consistent with fibrosis (F). No further surgery has been performed.

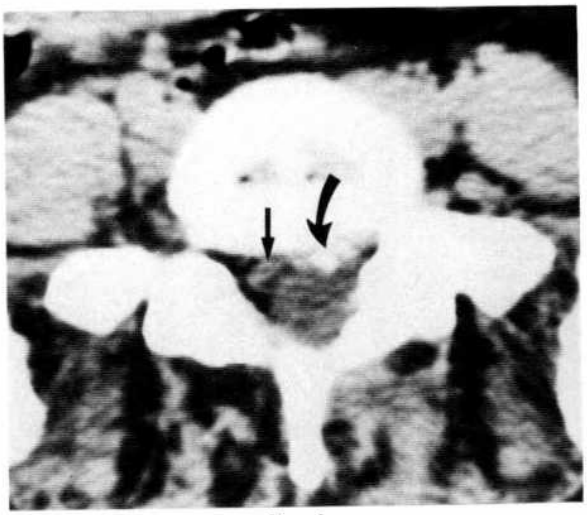


FIG. 6.

A CT cut through L5–S1 in a 37-year-old female in Group B. This study was performed 3 years following removal of the L5–S1 disc. The origin of the left S1 nerve root is completely obscured by a large, partly calcified abnormal structure (curved arrow). The right S1 nerve root is well seen (straight arrow). This lesion had a mean attenuation of 107 HU although some pixels reached 180 HU. Following enhancement, there was slight patient movement; the mean attenuation was 93 HU. This lesion was assessed as D, both before and after enhancement. A disc fragment was removed from this site at subsequent surgery.

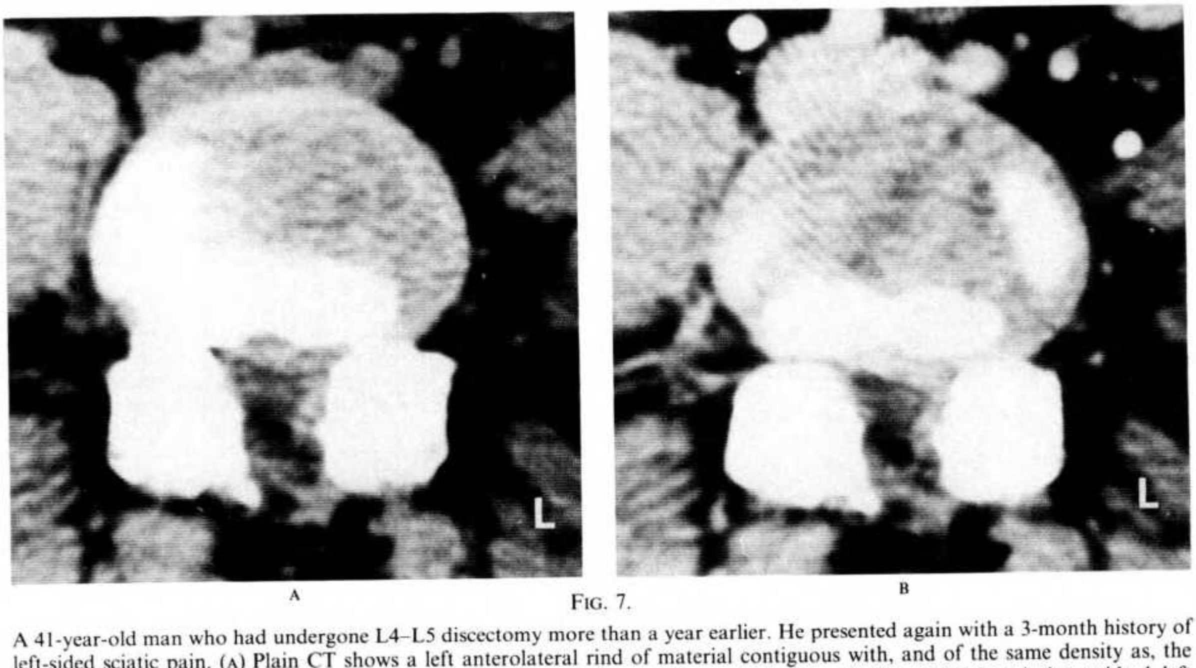
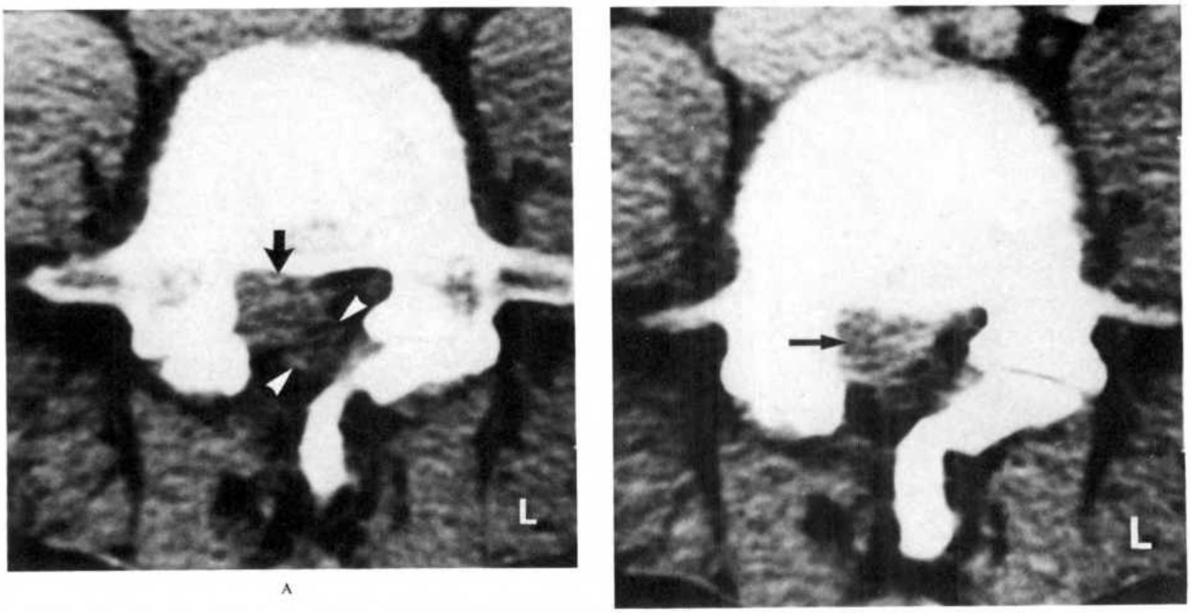


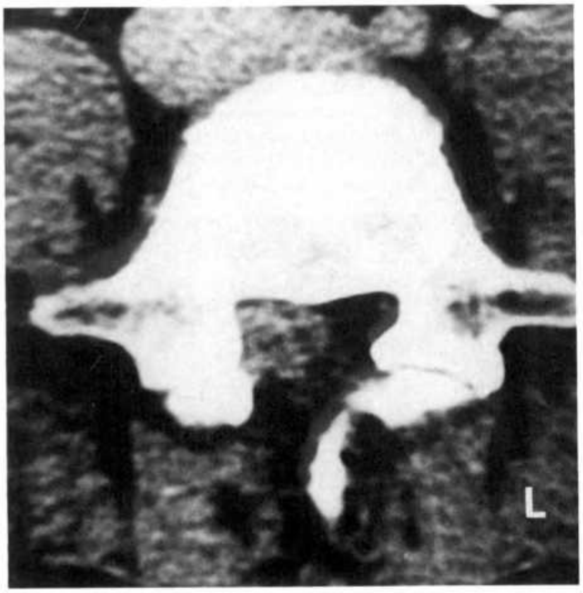
FIG. 7.

A 41-year-old man who had undergone L4–L5 discectomy more than a year earlier. He presented again with a 3-month history of left-sided sciatic pain. (A) Plain CT shows a left anterolateral rind of material contiguous with, and of the same density as, the disc (71 HU). There is a sharp interface with the adjacent theca. The combination of this material and the residual left ligamentum flavum is causing narrowing of the entry to the left lateral recess. This lesion was confidently diagnosed on this image as residual/recurrent disc material (D). The features were confirmed at surgery. (B) After 100 ml contrast medium there is little change in the appearances. After contrast medium the lesion measured 75 HU.



A

B



C

FIG. 8.

A 44-year-old female patient in Group C with recurring symptoms 8 months after L4–L5 discectomy. An example where some diagnostic problems remain even after 100 ml of contrast medium. (A) Non-enhanced image 8 mm caudal to the L4–L5 disc level. There is a large (1 cm) mass of soft tissue (black arrow, 70 HU) in the right lateral recess displacing the theca (arrowheads) posteriorly and to the left. The displacement and attenuation value favoured a disc lesion and there was little fibrosis elsewhere. However, the abnormality was quite caudal to the disc level, which appeared unremarkable. The features were considered equivocal (E). (B) Slight movement had occurred before enhanced views were obtained. This image, fractionally cranial to Figure 8A, shows some enhancement (+10 HU overall). However, the enhancement is non-uniform and could represent enhancement around a relatively avascular lesion/disc (arrow). (C) Fractionally caudal to Fig. 8A. Enhancement (+10 HU overall) is more uniform on this image. On balance, fibrosis was considered slightly more likely than a disc lesion (F > D). Perhaps there are two components to the lesion. The patient continues on conservative treatment. Follow-up CT would be helpful here to assess whether this lesion shrinks with time.

DISCUSSION

It is of little surprise that the attenuation values of those lesions considered to be due to fibrosis were lower (means ranging from 28 HU to 40 HU) than of those lesions considered to be due to disc material (means ranging from 65 HU to 81 HU, excluding one heavily calcified lesion of 300+ HU). This is, of course, one of the features used to distinguish fibrosis from disc material (Teplick & Haskin, 1983), although it is probably not as important as the site and shape of the abnormality itself (Braun et al, 1985). The attenuation values found in this series are generally rather lower than those reported by other workers (Teplick & Haskin, 1983): this probably reflects the fact that some of the abnormalities assessed were very small and, thus, measurements of attenuation were probably affected by partial volume effects.

The results also confirm that lesions considered to be due to fibrosis (F) enhanced while those considered to be due to disc material (D) did not enhance to any appreciable extent. It could be argued that this enhancement was used in the subjective classification of the abnormality in the 30 patients receiving contrast medium, and this is no doubt true in part. But comparison of Tables IIb and IId with Tables IIc and IIe shows that lesions considered on the *initial* pre-contrast assessments to be due to fibrosis enhanced in a similar fashion (mean gains +16 HU (Group B) and +23 HU (Group C)) when compared with those in whom the *final* radiological opinion was fibrosis (mean gains +12 HU (Group B) and +30 HU (Group C)).

It is interesting that the degree of enhancement of those lesions considered at the final assessment to be due to fibrosis was just over *double* when *double* the quantity of contrast medium was used (+30 HU in Group C versus +12 HU in Group B) (see Figs 3, 4). It would appear that other centres commonly use an even larger dose of contrast medium (often c. 50 g iodine), but as many employ a drip infusion technique after an initial loading bolus the precise amount used elsewhere is difficult to determine. The greater enhancement is certainly easier to display on hard copy and thereby easier for clinicians to appreciate; more subtle enhancement using the lower dose may only be evident on the monitor. However, this should not necessarily determine which dose is selected; we have shown that enhancement can be readily recognised using 16.25 g iodine (Fig. 3) and that there was little difference in the number of equivocal final interpretations between Groups B and C (after 50 ml and 100 ml, respectively). Perhaps, then, the lower dose could be used where enhancement is being used to confirm a strong suspicion of either disc material or fibrosis (F ≫ D/D ≫ F), reserving the larger dose for more equivocal appearances (F > D, E, D > F).

During the course of the study it became evident that the patient had often moved slightly between the pre- and post-contrast medium study of one level, despite instructions to keep as still as possible. Such movement was quite noticeable on several occasions. This problem has also been observed by other workers who advocate performing the venepuncture before beginning the procedure so that the risk of movement is diminished (Teplick & Haskin, 1984). Clearly, if the patient moves, comparison of pre- and post-contrast-medium data is not so accurate. However, such movement was occasionally beneficial by demonstrating slightly different anatomical features of a lesion than those seen initially, thus allowing a more confident opinion. It is already our normal practice to perform intervening cuts whenever an abnormality is seen or suspected. Perhaps even closer (*e.g.* 1 mm) intervals should be used over a small region where diagnostic uncertainty exists. The higher radiation dose would militate against such a policy as a routine.

In a normal lumbar spine, enhancement of the epidural veins is a characteristic feature. However, following surgery these veins usually are not well delineated due to their incorporation into the scar tissue. In this study the epidural veins were only well seen where the surgical intervention had been minimal (*e.g.* Fig. 1). Only occasionally did we observe enhancement at the circumference of an annulus or within a thickened theca (separate from perithecal fibrosis, *e.g.* Fig. 4) as described by others (Teplick & Haskin, 1984). This was probably due to the lower dose of contrast medium used by us.

We had hoped to compare the number of patients undergoing re-exploration in the three groups, but, as with other studies, there was a very low rate of re-exploration. In the event only eight of the 45 patients are known to have undergone re-exploration at the relevant site (three in Group A, two in Group B and three in Group C). In six of these eight patients disc material was confidently considered to be responsible for the abnormal appearances on CT (Grade D, Table I). A recurrent disc was found at surgery in four. In one patient the region of the disc was not well seen due to additional fibrosis (Group A); in the other no disc abnormality was found (Group C). Such a low rate of re-exploration prevents much comment as to the accuracy of the technique. In any case it should also be remembered that our analyses were often based on abnormalities which were not surgically significant (*e.g.* Fig. 3).

This study has confirmed the enhancing effect of contrast medium on lesions considered to be due to fibrosis. It has also shown that the degree of enhancement is dependent on the amount of contrast medium used. Although such enhancement contributed to a more confident radiological opinion at 13 out of 18 abnormal sites where the initial assessment was less than definite, the change was slight in 10 (Fig. 2). Interestingly, it never altered an initial radiological assessment of definite disc or definite fibrosis. The administration of contrast medium is considered to be an extremely useful adjunct whenever diagnostic uncertainty exists (24 out of 60 sites). However, it does not appear to be essential for every patient, especially when a radiologist is at hand to assess the routine findings on CT which may show normal appearances (12 out of 60 sites) or some definite abnormality (24 out of 60 sites).

ACKNOWLEDGMENTS

We are grateful to all the clinicians who referred patients to us and helped with follow-up information. We would also like to thank Dr T. D. Hawkins for his valuable advice. The Addenbrooke's Hospital Department of Medical Illustration and Photography prepared the figures. Alison Emery prepared the text.

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Correction

Hayward, S. J., McIvor, J., Burdge, A. H., Jewkes, R. F. & Williams, G., 1987. Staging of prostatic carcinoma with radionuclide bone scintigraphy and lymphography. *British Journal of Radiology, 60*, 79–81.

In the Results to this paper, on page 80, the opening sentence of the second paragraph should read "The incidence of metastases in patients staged clinically as T_3 and T_4 was significantly higher than in those staged as T_0, T_1 and T_2 ($p = < 0.005$, χ^2 with Yates' correction) (Table II)." The two percentages actually printed in the passage should have been deleted. We apologise for this error—would readers please correct their copies.

1987, *The British Journal of Radiology*, *60*, 223–230 MARCH 1987

Evaluation of pulmonary parenchymal disease by magnetic resonance imaging

By Mervyn D. Cohen, M.B., Ch.B., Richard L. Scales, M.D., *Howard Eigen, M.D., *Peter Scott, M.D., *Robert Tepper, M.D., David A. Cory, M.D. and John A. Smith, M.D.

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ABSTRACT

Thirty-eight patients with a wide variety of different disorders of the lung have been imaged using magnetic resonance. The disorders studied include congenital abnormalities, acute and chronic inflammation, vascular disorders, primary and secondary tumours of the lung, haematomas and infarcts. Magnetic resonance imaging identified all lesions seen on chest radiographs, but it is not quite as sensitive as computed tomography is for detection of very small abnormalities. Magnetic resonance may provide information to aid in differentiation of a wide variety of disorders causing diffuse pulmonary abnormality and might also prove helpful in differentiating acute inflammation from pulmonary collapse or fibrosis. In some disorders, such as lobar emphysema, cystic adenomatoid malformation and sequestration, the findings on the magnetic resonance scan alone will permit a correct diagnosis to be made in many cases. It is believed that magnetic resonance imaging has more potential for pulmonary imaging than has previously been recognised.

Magnetic resonance imaging (MRI) is gaining widespread recognition as a valuable method for the investigation of disorders of the central nervous system. It also has great promise for studying other regions of the body, including the musculoskeletal system, cardiovascular system, abdomen and pelvis, and can successfully image thoracic lymphomas (Cohen et al, 1983a,b; Gamsu et al, 1984; Webb et al, 1984; Cohen et al, 1985). There are isolated case reports of the ability of MRI to identify certain lung diseases such as pulmonary hypoplasia (Ross et al, 1984), pulmonary arterio-venous fistula (Guitierrez et al, 1984), metastases (Cohen et al, 1983a,b), and pulmonary embolus (Moore et al, 1984). Brasch et al (1984) have recently described the MRI of pulmonary abnormalities in six children with cystic fibrosis. This study reports the magnetic resonance findings in 38 children with a wide variety of lung disorders. Its objects were to see whether MRI could identify disease, to describe the magnetic resonance appearance of the disorders and to see how well it could differentiate the diseases.

METHODS

Thirty-eight children (aged 1 week to 15 years) were studied. In each case an abnormality had been detected on the chest radiograph before the magnetic resonance scan was performed.

Studies were approved by the Institutional Review Board.

All the scans were performed on a Technicare 0.15 T magnetic resonance unit. In all cases images were obtained in the transverse plane using T_1-weighted pulse sequences with a time to echo (TE) of 30 ms and a pulse repetition time (TR) of 500 ms. In almost every case additional images were obtained in either the coronal or sagittal plane. In every case additional images using a T_2-weighted pulse sequence were also obtained. The T_2-weighted pulse sequence had a TE of either 30 ms or 60 ms and a TR of either 1000 ms or 2000 ms. The magnetic resonance images were reviewed to see whether any abnormality could be identified, to localise any abnormality seen, and to compare the extent of abnormality seen with that seen on the chest radiograph. In addition, the change in image intensity between the T_1- and T_2-weighted pulse sequences was analysed to see whether the degree of change correlated with the disease process.

When sedation was required, chloral hydrate was given in a dose of 50–75 mg/kg body weight.

RESULTS

Table I lists the different disorders that have been studied and indicates the number of children with each disorder. Histological confirmation of the diagnosis was obtained in all those children with cystic adenomatoid malformation, lobar emphysema, lymphangiectasia, inflammatory pseudotumour, Letterer-Siewe disease, and tumour. It was also available for two of the patients with abscesses and one child with histoplasmosis. The sequestration was diagnosed from the chest radiograph and the diagnosis confirmed by angiography. The arterio-venous malformations were demonstrated by angiography. Cystic fibrosis was diagnosed by positive sweat tests and typical chest-radiograph findings. Pneumonia and abscess in two children were diagnosed by a typical clinical history and

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TABLE I

Diagnoses and number of patients studied

Pulmonary parenchymal disease	No. of cases
Congenital	
Cystic adenomatoid malformation	3
Lobar emphysema	3
Lymphangiectasia	1
Sequestration	1
Arterio-venous malformation	1
Inflammation	
Abscess	4
Pneumonia	4
Histoplasma	2
Miliary tuberculosis	1
Inflammatory pseudotumour	1
Allergic alveolitis	1
Letterer-Siewe disease	1
Vascular	
Congestive failure	4
Pulmonary infarction	1
Tumour	
Hodgkin's disease	2
Rhabdomyosarcoma	1
Metastases	3
Mechanical	
Collapse	3
Haematoma	1
Total	38

appropriate response to antibiotics. Diffuse pulmonary histoplasmosis was diagnosed by high antibody titres to *Histoplasma capsulatum*. Miliary tuberculosis was diagnosed by culture of microbacteria tuberculosis from the mother and by a positive skin-test in the baby. Congestive cardiac failure was diagnosed clinically. Pulmonary infarction was diagnosed from clinical and chest-radiograph findings in a patient with sickle-cell anaemia. Pulmonary collapse was diagnosed on the chest radiograph. Haematoma was diagnosed from the chest radiograph in a patient with a history of trauma.

Magnetic resonance scanning was well tolerated by the children and no complications were encountered.

Cystic adenomatoid malformations (Figs 1, 2) had varied definition of their margins, and were non-homogeneous with signals of varying intensity seen on both T_1- and T_2-weighted images. This is because of the mixed pathology, which includes air- and fluid-filled cysts and soft-tissue masses.

Lobar emphysema (Fig. 3) appeared as a region of very low intensity on both T_1- and T_2-weighted images and the signal obtained from the emphysematous lobe was lower than that obtained from adjacent lung. The margins of the abnormality were sharply defined, and varying degrees of mediastinal shift could be identified. Asymmetry of the right and left hemithorax could also be identified owing to expansion of the chest wall by the underlying emphysema.

Lymphangiectasia (Fig. 4) appeared as a diffuse, grainy granularity in both lung fields, with superimposed tubular structures most easily seen on T_2-weighted images. No definite nodules could be identified. The T_2-weighted image showed a very strong signal from these tubular structures, much greater than that of fat. This suggests the presence of fluid, probably lymph, with a very long T_2-relaxation time.

The pulmonary sequestration (Fig. 5) was identified in the left lower lobe. It had margins which were moderately well defined and an irregular internal structure due to the presence of soft-tissue and air cysts. The soft-tissue component had an intensity similar to muscle on the T_1 image and similar to liver on the T_2 image. No fluid was identified in the sequestration. A digital subtraction angiogram identified a large feeding vessel arising from the abdominal aorta, passing through the diaphragm into the sequestration. This vessel could also be seen on MRI.

The patient with arterio-venous malformations (AVMs) had hundreds of diffuse small AVMs in both lung fields. The diagnosis was made by the demonstration of intrapulmonary shunts using radionuclide-labelled, albumin microspheres and it was confirmed by angiography. On the magnetic resonance image the individual vascular malformations could not be identified. There was, however, a diffuse abnormality with strong signal from the pulmonary vessels. This is believed to be because of paradoxical enhancement from slow flow through distended pulmonary vessels.

All of the acute bacterial infections (Figs 6, 7) showed a similar appearance. The margins of the infections were well defined when they touched a fissure, but were otherwise poorly defined. All had a signal intensity much greater than that of normal lung and on the T_1-weighted images varied from just below to just above

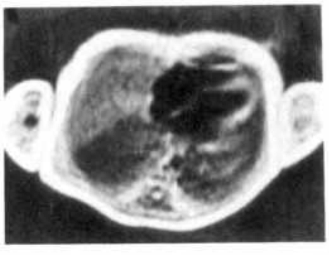


Fig. 1.

Cystic adenomatoid malformation. Transverse image, with TE = 30 ms and TR = 500 ms, reveals a fairly homogeneous abnormality of the middle lobe. The signal intensity is greater than that of normal lung and the lobe is expanded. This image was taken through a predominantly soft-tissue component of the malformation.

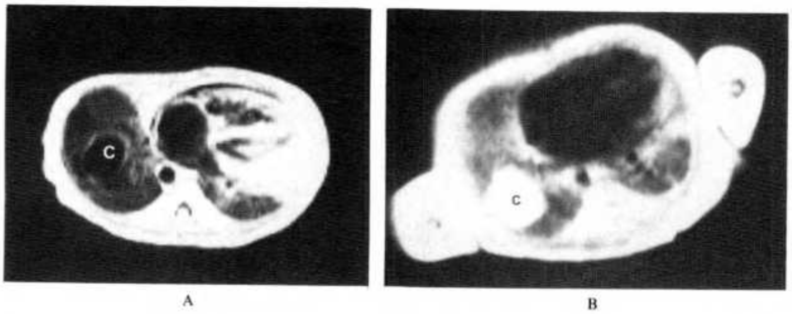


FIG. 2.

Cystic adenomatoid malformation. Transverse images, (A) TE = 30 ms and TR = 500 ms and (B) TE = 60 ms and TR = 1000 ms. Images are obtained through a cystic adenomatoid malformation in the right lower lobe. On the T_1-weighted image (A) the cystic component of the abnormality (C) has a very low intensity but is of very high intensity on the T_2-weighted image (B). The margins of the soft-tissue component of the abnormality are very poorly defined.

that of muscle. All showed strong increase in signal intensity on T_2-weighted images with the signal increasing to that of fat or just below fat. Abscess cavities (Fig. 6) were identified in four patients, the walls of the abscesses varying from very thin to thick. The thick walls showed only slight increase in signal intensity from T_1- to T_2-weighted images. Air in the abscess cavities was identified by very low signal intensity on all pulse sequences and appeared similar to air in adjacent normal lung. Fluid in one abscess cavity had a very strong signal on the T_2-weighted image and a moderately strong signal on the T_1-weighted image, both signals being much greater than that from adjacent chest wall muscle. Two of the three patients with cystic fibrosis had acute pneumonia diagnosed by chest radiography, clinical findings and response to antibiotics and the pneumonia appeared no different from that in patients without cystic fibrosis. The lungs in the three patients showed only mild changes of cystic fibrosis with hyperinflation and prominence of bronchovascular markings, and no large areas of atelectasis.

Miliary tuberculosis appeared as a coarse granularity

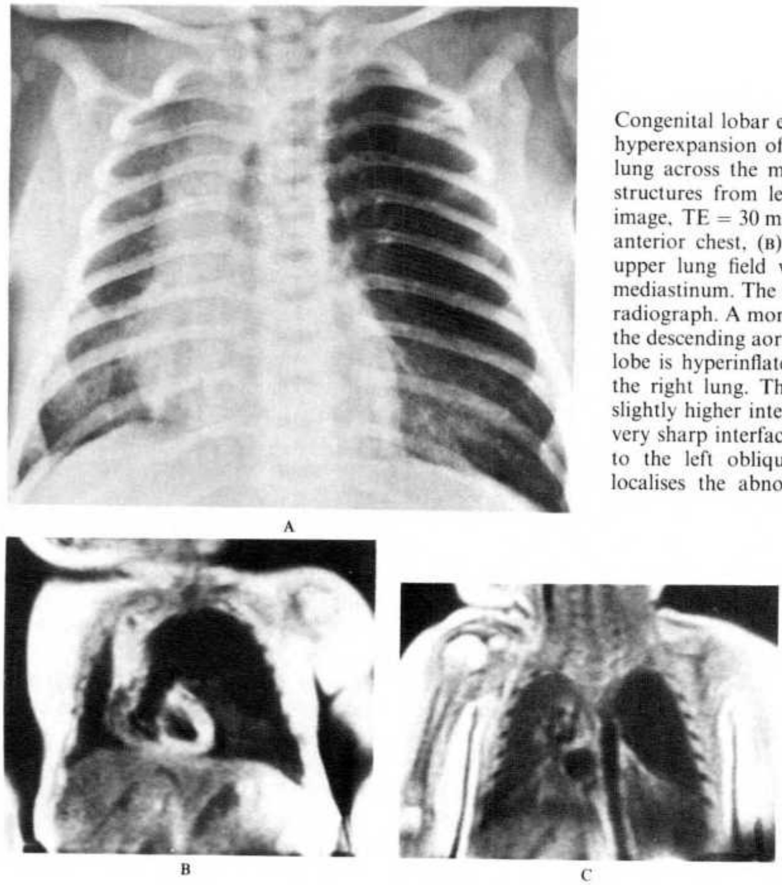
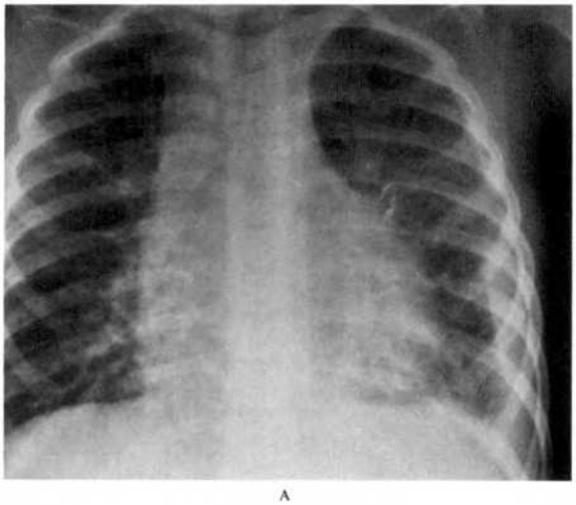


FIG. 3.

Congenital lobar emphysema. The chest radiograph (A) shows hyperexpansion of the left upper lung field with herniation of lung across the midline and displacement of the mediastinal structures from left to right. A coronal magnetic resonance image, TE = 30 ms and TR = 1000 ms, obtained through the anterior chest, (B) shows marked hyperexpansion of the left upper lung field with significant displacement of heart and mediastinum. The appearance corresponds to that on the chest radiograph. A more posterior image (C) obtained at the level of the descending aorta delineates the abnormality. The left upper lobe is hyperinflated and of much lower signal intensity than the right lung. The partially collapsed left lower lobe has a slightly higher intensity than the normal right lung. There is a very sharp interface between the upper and lower lobes owing to the left oblique fissure. The magnetic resonance image localises the abnormality more clearly than does the chest radiograph.



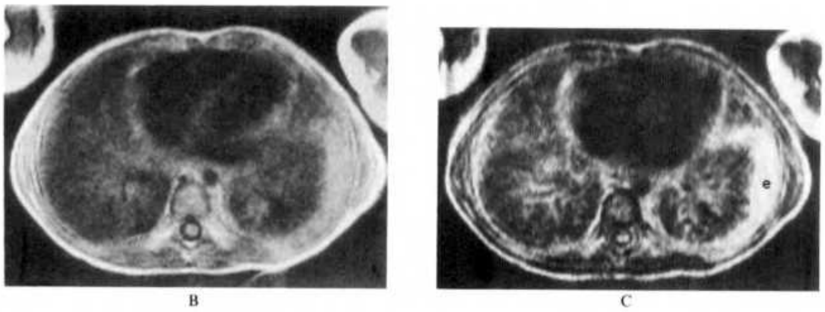


FIG. 4.

Lymphangiectasia. The chest radiograph (A) demonstrates a mild diffuse reticulo-nodular abnormality in both lung fields. Clips are shown in the left lung at the site of biopsy and there is a left pleural effusion. A moderately T_2-weighted image (B), with TE = 60 ms and TR = 1000 ms, shows a diffuse granular abnormality throughout both lung fields. The effusion is seen as a region of intermediate intensity between that of soft tissue and muscle. A very strongly T_2-weighted image (C), with TE = 120 ms and TR = 2000 ms, shows diffuse abnormality in the base of the lung much more sharply defined than on the chest radiograph. The appearance has changed significantly compared with the moderately T_2-weighted image, possibly as a result of enhancement of the signal intensity from fluid in distended lymphatics. The pleural effusion (e) now gives a very strong signal intensity, presumably because of the prolonged T_2 relaxation time of the fluid.

with good definition of the lung nodules. On the T_1-weighted images their intensity was similar to muscle and it increased significantly on T_2-weighted images to just below that of fat. Enlarged hilar and tracheal lymph nodes could be distinguished. The patients with diffuse pulmonary histoplasmosis had only hazy, ill-defined nodules on the magnetic resonance image, which were less well identified by MRI than by chest radiography. This was the only disease in which MRI was less revealing than a chest radiograph. The signal intensity from the nodules was much less than that of muscle on the T_1-weighted image with moderate increase on the T_2-weighted image and the nodules were much less well defined than in tuberculosis. Enlarged hilar and mediastinal lymph nodes were identified and these increased in intensity on the T_2-weighted image. In the patient with chronic histoplasmosis of the left upper lobe and hila there was displacement and narrowing of the trachea and left main-stem bronchus from the enlarged lymph node. The left upper lobe mass revealed an intensity similar to muscle on T_1-weighted image and the image had a fairly homogeneous intensity. On the T_2-weighted image the intensity was very unhomogeneous with some regions having an intensity just greater than that of muscle, other areas being brighter and similar to fat. This corresponded well with the findings on examination of the pathology specimens which revealed regions of granuloma, inflammatory infiltrate and fibrosis.

Letterer-Siewe disease had a hazy, uniform, ground-glass appearance throughout both lung fields and no individual nodules could be identified. The intensity was slightly less than muscle on the TE 30 ms, TR 500 ms image. There was slight increase in signal on the T_2-weighted image but the intensity remained much less than that of fat and the change in intensity was much less than that seen in tuberculosis. This patient also had an inversion-recovery image performed which showed a signal intensity similar to that on the spin-echo image with TE = 30 ms and TR = 500 ms.

The inflammatory pseudotumour was found to be compressing the origin of the right middle lobe bronchus. Both the tumour and the collapsed middle lobe appeared of similar intensity on both T_1- and T_2-weighted images and there was only very slight increase in intensity from the T_1- to the T_2-weighted image.

Segments of pulmonary collapse (Fig. 8) appeared as well defined abnormalities showing less increase in signal intensity from T_1 to T_2 images than acute pneumonia.

The lung haematoma appeared as a moderately well defined region of strong intensity on both T_1- and T_2-weighted images.

Pulmonary oedema (Fig. 9) appeared as a hazy

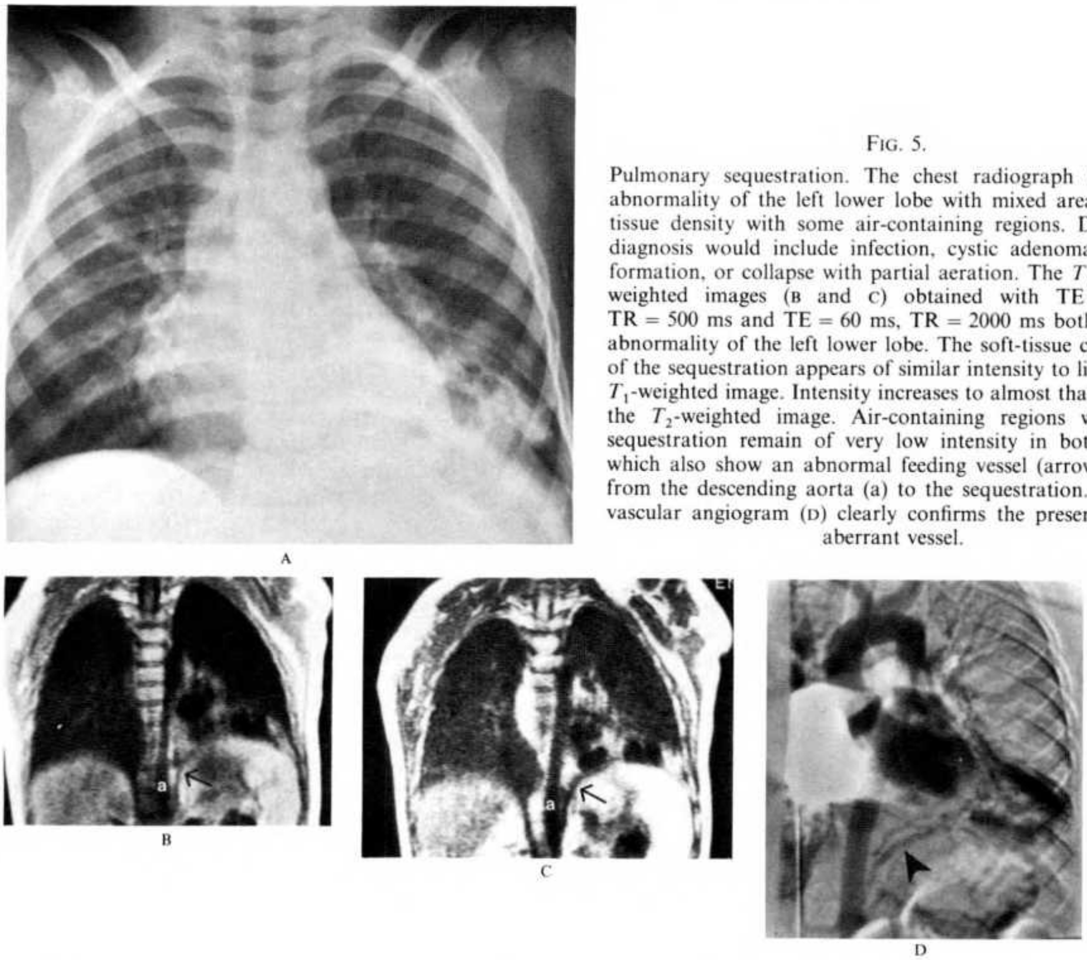


FIG. 5.

Pulmonary sequestration. The chest radiograph (A) shows abnormality of the left lower lobe with mixed areas of soft-tissue density with some air-containing regions. Differential diagnosis would include infection, cystic adenomatoid malformation, or collapse with partial aeration. The T_1- and T_2-weighted images (B and C) obtained with TE = 30 ms, TR = 500 ms and TE = 60 ms, TR = 2000 ms both show an abnormality of the left lower lobe. The soft-tissue component of the sequestration appears of similar intensity to liver on the T_1-weighted image. Intensity increases to almost that of fat on the T_2-weighted image. Air-containing regions within the sequestration remain of very low intensity in both images, which also show an abnormal feeding vessel (arrow) passing from the descending aorta (a) to the sequestration. A digital vascular angiogram (D) clearly confirms the presence of the aberrant vessel.

granularity varying in texture from fine to coarse. When obtained, coronal images showed very clearly the perihilar distribution of the abnormal fluid in the lungs as well as cardiomegaly and pleural effusions. The effusions were best characterised by persistence of a strong signal on images with very long TEs on multiecho acquisition sequences.

Several different intrapulmonary tumours were identified. A large fibrillary inclusion-body sarcoma appeared as a well defined mass with sharp margins. The signal intensity was almost homogeneous apart from a very small focus of low intensity on the T_1-weighted image and very high intensity on the T_2-weighted image. The main bulk of the tumour had a strong intensity on the T_2-weighted image, much greater than that of muscle but less than that of fat. On the T_1-weighted image the intensity was similar to muscle. Magnetic resonance was much better than CT at differentiating the mass from the adjacent heart. Patchy lung nodules were identified in two patients with

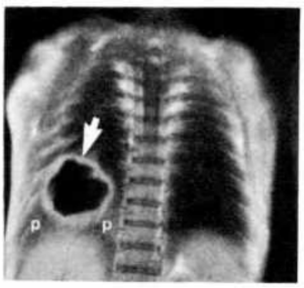


FIG. 6.

Abscess. The TE = 30 ms and TR = 500 ms image identifies a large abscess in the right lower lobe with a thick wall (arrow) of moderately strong intensity. This intensity did not change greatly on T_2-weighted images. Adjacent pneumonia (p) is seen as a hazy, moderately low-intensity, ill-defined region. The signal intensity from the pneumonia increased significantly on T_2-weighted images.

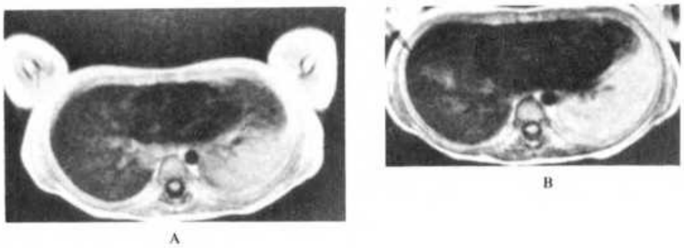


FIG. 7.

Staphylococcal pneumonia. Transverse T_1 (A) and T_2 (B) images with TE = 30 ms, TR = 500 ms and TE = 60 ms, TR = 1000 ms, respectively. Both show an area of diffuse abnormality in the left lower lobe. The signal intensity from the pneumonic consolidation is similar to that of muscle on the T_1-weighted image. On the T_2-weighted image it increases significantly to become almost as white as fat. An air bronchogram is better appreciated on the T_1-weighted image.

Hodgkin's disease but were less well identified using MRI than CT. In one of these patients, the T_2 image revealed streaky regions of high intensity radiating from enlarged hilar lymph nodes to the peripheral lung nodules. This infiltrating disease, seen with MRI, was not appreciated on CT. Metastases in one patient with osteogenic sarcoma (Fig. 10) and one with Wilm's tumour appeared similar. They were seen as moderately sharply defined nodules with intermediate intensity on T_1 images and very strong intensity on T_2 images. In another patient with osteogenic sarcoma, small metastases (mostly under 0.5 cm in diameter) were seen on the CT scan but could not be identified on either T_1- or T_2-weighted magnetic resonance images.

DISCUSSION

On normal magnetic resonance images the heart, major mediastinal blood vessels, trachea and the main-stem bronchi can all be easily seen (Gamsu et al, 1983; Jones et al, 1984). More peripheral bronchi are not seen as easily on CT scans (Webb et al, 1984). The right and left pulmonary arteries can also be identified. In the lungs there is a very low signal. A hazy background branching network can often be seen (O'Donovan et al, 1984) but fissures are not routinely identified (O'Donovan et al, 1984). One advantage of MRI is the ability to image in multiple planes. Coronal and sagittal planes have been reported as being helpful in evaluation of the mediastinum (O'Donovan et al, 1984; Webb et al, 1985) and the coronal plane corresponds to that of the conventional chest radiograph (O'Donovan et al, 1984). In the lungs themselves these planes may also be useful: they help to show the distribution of diffuse abnormality in the lung fields, to localise abnormality anatomically within the lungs, to show associated disorders such as left-atrial enlargement in congestive

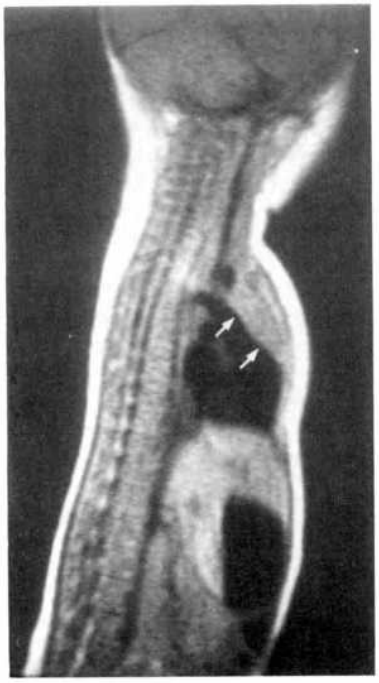


FIG. 8.

Left upper lobe collapse. Sagittal image with TE = 30 ms and TR = 500 ms shows the left upper lobe to be significantly reduced in volume and to lie obliquely in the upper mediastinum. The oblique fissure (arrows) is displaced forwards and upwards.

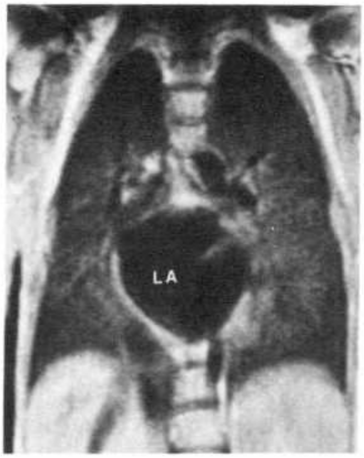


FIG. 9.

Pulmonary oedema. The coronal gated image with TE = 30 ms as obtained at the level of the left atrium. The patient had complex congenital heart disease including severe mitral regurgitation and pulmonary oedema. The left atrium (LA) is grossly enlarged. The pulmonary oedema is seen as an increased signal intensity from both lungs, maximal in the perihilar areas.

cardiac failure as well as enlarged hilar and paratracheal lymph nodes in tuberculosis, lymphoma and histoplasmosis.

Magnetic resonance imaging has proved effective at demonstrating abnormality. In every patient, disease seen on chest radiography was demonstrated by MRI. In one patient MRI could not identify small metastases, from an osteogenic sarcoma, seen on chest CT but not on a radiograph. The only time when MRI showed less abnormality than the chest radiograph was in a patient with diffuse pulmonary histoplasmosis, but the reason for this is not evident.

Magnetic resonance imaging of the lungs requires utilisation of at least two pulse sequences. The characterisation of tissue is greatly helped by observing the change in intensity of signal from the tissue when different pulse sequences are utilised. In most of our patients we used only two pulse sequences. More recently we have been able to obtain multislice multiecho acquisition simultaneously, permitting simultaneous acquisition of images with up to eight different TEs and the same TR. This, in a few cases, has proved helpful. For example, fluid may have a longer T_2 relaxation time than fat and invariably has a longer T_2 relaxation time than tumour or inflammation. This is appreciated as persistence of a strong-intensity signal on images with a very long TE (in the range 150–240 ms). The results of our study suggest that the amount of increase in signal intensity on the T_2 image may help to differentiate some disorders. The acute infections and tumours showed greater increase in signal intensity on T_2 images than did collapsed lung, an inflammatory pseudotumour, and fibrosis seen in chronic histoplasmosis. Thick abscess walls showed similar changes. Some disorders had characteristic appearances, permitting diagnosis to be made by MRI alone. Cystic adenomatoid malformation showed a much wider range of signals than the other disorders and this could prove helpful in the diagnosis of the disorder. In lobar emphysema the signal intensity is lower than that of normal lung and the distribution of the abnormality corresponds to that of a lung lobe.

Breathing has not produced significant artefacts in our patients, despite the lack of respiratory gating. Other workers have reported similar findings (Gamsu et al, 1983). The resolution in MRI is not quite as good as that in CT, and small nodules in the lungs can be missed by MRI (Balthazar et al, 1985).

Magnetic resonance imaging may have a role to play in the differentiation of diffuse pulmonary disorders. Although we have studied only a few such patients, the appearance in miliary tuberculosis, diffuse histoplasmosis, histiocytosis, pulmonary oedema and allergic alveolitis does show a difference between these disorders. Further studies with a larger number of patients are needed to explore further this potential use for MRI.

In conclusion, MRI can identify a wide variety of different disorders of the lungs. Optimal MRI requires a range of imaging pulse sequences in more than one body plane. In some disorders MRI alone can permit a diagnosis to be made; in others it may add new information; it helps in the differentiation of diffuse pulmonary disorders and also in the distinction of acute

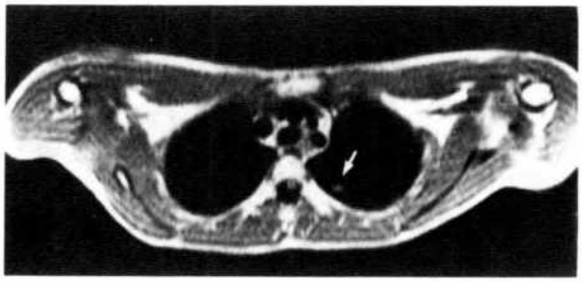


FIG. 10.

Osteogenic sarcoma: lung metastasis. This shows on the TE = 30 ms and TR = 500 ms transverse image as a single, nodular density in the left lung (arrow).

inflammation from fibrosis or collapse. The overall sensitivity of MRI for the detection of small lesions remains less than that of CT. Although the exact clinical utility of MRI remains unknown, the results of this study suggest that it may have a greater role to play in pulmonary imaging than has previously been recognised.

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Cancers induced and cancers detected in a mammography screening programme

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ABSTRACT

The numbers of cancers which might be induced in a breast screening programme are compared with the numbers detected. The induction rate is estimated from reports of breast cancer in various groups exposed to high radiation doses, and also from International Commission on Radiological Protection risk estimates. An apparent discrepancy between these two approaches is discussed and removed. Detection rates are based on preliminary results in Edinburgh, and greatly exceed the induction rate. Whether such an excess is maintained if an X-ray grid requiring a higher dose is used on younger age groups is discussed.

In a screening programme for breast cancer in symptom-free women, using mammography, it is essential that the number of unsuspected cancers detected should exceed the number of future cancers induced. It is desirable that the excess should appear to be large, since the cancer induction rate can only be estimated with some uncertainty, and some of the detected cancers might have been detected by other means within a short time.

The problem may be approached by considering the probability of an unknown cancer being detected and cured, and then estimating probable lengthening of life. The probability of future cancer induction can similarly be represented by a probable shortening of life. This involves some obvious uncertainties, including those from the statistical analysis of treatment results. An alternative approach, which reduces the number of uncertainties and their total magnitude, is simply to compare the number of cancers detected with the probable number of cancers induced in the future. If induced cancers are in no way discounted for being future events, and if it is assumed that the probability of detection and cure in the future is the same as at present, then a straight comparison of numbers may be meaningful. It seems unreasonable to suppose that detection and the results of treatment will become worse with time, so this assumption tends to underestimate any benefit which may arise.

It is that approach which will be followed in this paper. Substantial uncertainties will remain, at least in estimates of cancers induced, but the overall uncertainty is likely to be less than for alternative methods.

There is much public fear of radiation, in any kind or quantity, and this fear is spreading among medical workers. In comparisons between any new diagnostic modality and radiology, X rays are frequently described as hazardous, regardless of dose involved or diagnostic accuracy. It is essential that benefit and detriment are both seen in correct perspective.

ESTIMATES OF CANCERS INDUCED

(a) *The number of cancers induced per unit dose*

Most authors discuss the problem in terms of excess cancers per unit dose, though occasionally a paper will consider the possibility that radiation multiplies the natural incidence rather than merely adding to it. The former approach will be followed here, as reflecting the general practice in the literature. A number of papers and reviews consider the excess cancers from a variety of medical procedures and from occupational exposure, and these are supplemented by data from atomic-bomb survivors. A brief review of a very few of these is given by Boice and Monson (1977) and a fuller review is found in the report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) for 1977. These papers usually provide estimates of excess cancers per rad per million woman-years (WY) at risk and the numbers are of a convenient size. To conform with SI units while keeping the numbers the same, excess cancers per 10^4 WY-Gy may be considered.

Boice et al (1979) derive estimates, from three medical procedures, of 6.2 to 8.4 excess cancers per 10^6 WY-rad, but only 3.6 per 10^6 WY-rad from atomic-bomb survivors. UNSCEAR (1977) review a wider range of sources but settle for 6–8 per 10^6 WY-rad as their best estimate. The Commission on the Biological Effects of Ionising Radiation (BEIR, 1972), quoted in Boice et al (1979), estimates six cases per 10^6 WY-rad. Feig (1984) quotes estimates by the National Cancer Institute of 7.5 excess cancer cases per 10^6 WY-rad for women exposed below age 35 years and 3.5 excess cases for those exposed at age 35 years or above. Women undergoing mammography are seldom as young as 35 years, and present policy on screening of symptom-free women in the UK does not go below age 45 years. The best estimate for the present purpose seems to be about six cases per 10^6 WY-rad.

Translating this into a lifetime risk for a woman of a given age depends on our expectation of when the excess cancers will appear. There seems to be general agreement that very few if any will appear in the first 10 years post-irradiation, with a build up over the next 10 years. Feig (1984) suggests that this latent period is longer in younger women. Some writers assume that there is a time within which all the resulting cancers will have appeared and the following 30 years is sometimes taken as this period. However, this assumption may no longer be warranted (Feig, 1984).

In apparent contrast to this kind of analysis, the International Commission on Radiological Protection (ICRP, 1977) has deduced an estimate of the lifetime risk of breast cancer to a population receiving unit dose, and this and similar figures for other cancers are often quoted. This seems to be a more convenient quantity since our aim is an estimate of the future risk to a screened population. The ICRP estimate of lifetime risk is 25 per 10^6 per rad, though no details of how this figure was derived appear to have been published. At first sight this seems to be a much lower estimate than in the preceding paragraph, since six cases per 10^6 WY-rad, spread evenly over 10 to 40 years post-irradiation, appears to represent a lifetime risk of 180 cases per 10^6 per rad. Before proceeding further, these numbers need to be reconciled.

The ICRP figure is for a million population of both sexes and all ages. Moreover, this is an estimate of fatal cancers, whereas the other sources are estimating cancer cases. Estimates of the proportion of breast cancer cases which prove fatal are also variable. UNSCEAR (1977) quote mortality values as low as 0.2 of incidence rates, but up to 0.45. The best currently available figure for 5-year survival is 57% based on data from the Office of Population Censuses and Surveys (OPCS). However, the 5-year survival concept of "cure" seems much less applicable in breast than in some other forms of cancer. An assumption that on average about half the cases prove fatal seems reasonable. Taking this value transforms the ICRP figure from 25 per 10^6 population per rad to 100 cases per 10^6 women per rad. It is then necessary to allow for the age distribution of the population and the fact that not all members of a random population sample would live long enough to develop the cancers induced by a radiation exposure, or a series of such exposures. An example of the kind of calculation involved is given by Boice et al (1979). A very simple approach is illustrated in Table I, which assumes a population uniformly distributed in age up to 70 years, a mean expectancy of age 75 years at death, and cancers arising uniformly at six cases per year from 15 to 40 years post-irradiation to 1 rad. Thus, *on these crudely simplified assumptions*, the apparent discrepancy can be removed entirely.

TABLE I

BREAST CANCERS PER 10^6 WOMEN-RAD FOR DIFFERENT AGES AT TIME OF IRRADIATION

Age group (years)	Assumed mean lifetime expectancy (years)	Excess cancers per 10^6 woman-rad
0–10	70	150
10–20	60	150
20–30	50	150
30–40	40	150
40–50	30	90
50–60	20	30
60–70	10	0
		Mean 103

The above calculation assumes there is no variation in risk with age of the woman at exposure. This, however, is a point of some controversy, as will be seen from the review of UNSCEAR (1977). Shore et al (1977) and Boice and Monson (1977), in consecutive papers of the same journal number, do not agree, the latter claiming higher risk at younger exposure (independent of life expectancy) while the former claim no difference at least up to age 45 years. UNSCEAR (1977, para 181) interpret the figures of Shore et al (1977) as implying a slightly increased risk for those over age 30 years, but Shore et al do not necessarily accept that implication themselves. Baverstock et al (1981), discussing women luminisers, clearly say "radiation induced breast cancer is associated particularly with younger women and with a long latent period" and go on to imply that women over age 30 years at exposure are at lower risk. The National Cancer Institute figures quoted by Feig (1984) have already been referred to: 3.5 cases/10^6 WY-rad above age 35 years but 7.5 below that age.

To assess risks in mammography, it seems prudent at present to assume:

(a) six cases per million per year per rad;
(b) cancers arising uniformly from 10 years post-irradiation for the whole of life;
(c) no variation in risk with age at exposure.

These assumptions, together with life expectancy figures from OPCS, are used in Table II to estimate excess cancers for various ages at exposure. The results are believed to overestimate the true numbers for the

TABLE II

ESTIMATED EXCESS BREAST CANCERS PER mGy PER 10^6 WOMEN OF SCREENING AGE, ON SPECIFIED ASSUMPTIONS (SEE TEXT)

Age at exposure (years)	Life expectancy (years)	Excess cancers per 10^6 per mGy
35	41	18.6
40	36	15.6
45	32	13.2
50	27	10.2
55	23	7.8
60	19	5.4
65	16	3.6

reasons stated, and also because they are based on extrapolation from high doses to low ones. Roebuck (1986) has pointed out in a timely reminder that, if low doses of radiation do cause cancer, the incidence is so low that it has never been observed.

(b) Radiation dose in mammography

For various technical reasons (low kV for contrast, slow films for definition, short focus–screen distance) mammography has, in the past, required a surface dose of several rads. Technical advances in recent years, especially the general use of intensifying screens, have reduced doses very substantially, yet mammography is still too often regarded as a high-dose procedure. The advent of xerography some years ago, with its apparent gain in image quality, may have helped to perpetuate this belief, since it does require a relatively high dose. However, molybdenum target tubes with molybdenum filters, used with the best film–screen combinations vacuum packed, now seem able to give image quality at least as good as xerography at much lower doses, and the current trend is away from xerography. Other target and filter materials may also be available, and fresh films and (to a lesser extent) screens are always coming onto the market.

With these techniques, mammography doses are now of the order of a few mGy to the entrance surface, and around 1 mGy as an average through the breast (20–25% of surface dose at 25–28 kV). These figures, it must be emphasised, are for an average breast under compression and about 5 cm thick. For larger breasts of, say, 8 cm, surface dose may well be over 10 mGy (1 rad) and if a moving grid is used on such a breast (which is where it is most valuable) the surface dose will be greater again and the mean breast dose may be of the order of 10 mGy.

In assessing risks from mammography in the past, surface dose has most often been used, perhaps because it represented an upper limit or because it was easy to measure. However, the average dose throughout the breast seems likely to provide a better criterion. (Energy imparted to the breast may be better still but all the literature on risk estimates is in terms of dose or exposure. That literature is also based on much more penetrating radiation than that now used in mammography, giving more uniform dose.) On this basis and the assumptions above, the expected numbers of cancers caused are as shown in Table III. It is worth emphasising that these numbers are very small. In a screening programme covering a population evenly distributed between ages 45 years and 65 years, and for whom a grid was used in 10% of films, to induce a single cancer would, on a statistical basis, require about 70 000 films at the doses given here.

In assessing risks from breast doses, there seems little point in arguing questions such as whether to use grays in breast tissue or grays in water, or the proper allowance for dose scattered from the opposite breast, or the detailed accuracy of the dosemeter calibration, each of which may contribute a correction of around 10%. Risk estimates are almost certainly based on exposure or on doses which are grays in water.

TABLE III

Expected breast cancers induced by typical mammographic doses

Age (years)	Average breast mean dose 1 mGy	Thick breast with grid mean dose 10 mGy
35	19	186
40	16	156
45	13	132
50	10	102
55	8	78
60	5	54
65	4	36

Notes. (1) If surface dose were used as the criterion, these numbers would need to be multiplied by 4 or 5. (2) Current UK screening practice is to screen from age 45 years to 65 years. Figures for 35- and 40-year-old women have been included for illustration.

Breast Cancer Detection Rates

As with mammography doses, these can be expected to vary to some extent between centres. They will certainly tend to vary with age of the patients. An added complication, at least from an ethical viewpoint, is that where other detection methods (such as clinical examination) are used as well as mammography, some cancers will be detected without the aid of mammography. However, if a future screening programme is planned based on mammography alone, experience suggests that this will detect over 90% of cancers detected by all methods combined.

If a screening programme included repeat examinations at later intervals, it is likely to detect rather more cancers at the first examination (prevalence) than at later ones (incidence). Detection rates to be used here are set out in Table IV, and are based on preliminary results observed in Edinburgh, which is one of the four centres in the UK trial for early detection of breast cancer. Those for the first examination are actual rates rounded to the nearest whole number, while those for second examinations (2 years later) represent a uniform

TABLE IV

Preliminary breast cancer detection rates from Edinburgh centre of UK trial

Age range (years)	Breast cancer detection rates per 1000	
	First examination (two films)	Second examination (single film)
45–49	4	2
50–54	5	2
55–59	5	2
60–64	9	2

TABLE V

RATIOS OF BREAST CANCERS DETECTED TO BREAST CANCERS INDUCED, EDINBURGH PRELIMINARY RESULTS

Age range (years)	Cancers detected/cancers induced	
	First examination (two films, dose 2 mGy)	Subsequent examinations (one film, dose 1 mGy)
45–49	170	170
50–54	280	220
55–59	380	310
60–64	1000	440

estimate for all age groups, based on Edinburgh trial experience so far.

Current Edinburgh doses, for a 5 cm compressed breast, are around 1 mGy per film averaged through the breast. At the first examination two films per breast are routinely taken, but only one per breast at subsequent examinations. Applying these doses to the figures of Table III, and using the detection rates of Table IV, gives ratios for cancers detected/cancers induced as shown in Table V. The ratios have been rounded to two significant figures. Greater precision would not be justified in view of the underlying assumptions.

DISCUSSION

The ratios are very high in all cases. Even if the dose were 10 times higher, for example if a grid was used on a thicker breast, they would still be high. These ratio values carry an appreciable uncertainty, arising from (a) the risk estimates (up to a factor of 1.5), (b) dose estimates (factor of about 1.5) and (c) detection rates, since these are statistical and will not be precisely reproducible (around a factor of 2). Nevertheless, even a combination of these errors all in the wrong direction, and on a 45-year-old patient on whom a grid was used, would still not reduce the ratio to unity. As already pointed out, the induction rates are thought to be overestimates.

Younger patients may be included in some screening programmes overseas, but detection rates at younger ages are difficult to predict reliably. Cancer induction rates at age 35 years and 40 years are estimated in Table III. For a dose per film of 1 mGy, a detection rate as low as 0.02 per 1000 would still be likely to exceed the induction rate, and for a dose of 10 mGy per film a detection rate of 0.2 per 1000 would have the same effect. However, if full allowance is made for the various uncertainties, the detection rate at age 35 years might need to be as high as one per 1000 if a grid were to be used at a dose of 10 mGy and still give an excess of cancers detected over cancers induced.

Thus, if screening were to be extended down to age 40 years the ratio would almost certainly still be satisfactorily high for all but the thickest breasts, for which dose reduction techniques would be more than usually important and comparable in importance with measures to improve diagnostic accuracy. Use of a grid in women of this age would need careful consideration. Screening from age 35 years, using present techniques and including grids, might present ethical problems.

At the present screening age range in Britain, it seems reasonable to attach primary importance to diagnostic accuracy, with dose reduction always having an important but secondary role. *The Lancet* in April 1985, discussing recently reported results of screening in Sweden, remarked "Its principal disadvantage is not the miniscule radiation hazard but... overtreatment" (Anonymous, 1985) and this view seems to be confirmed by the figures presented here.

Risk estimates are constantly being reviewed, as are diagnostic techniques, and both need to be closely watched. Further information would be particularly valuable on:

(a) age dependence of the estimate of risk,
(b) whether excess cancers due to radiation continue to arise throughout the woman's lifetime,
(c) whether there is a longer latent period for younger women, and
(d) age dependence of the screening detection rate.

ACKNOWLEDGMENTS

I am grateful to Dr Freda Alexander for showing me the preliminary cancer detection rates from the Edinburgh arm of the UK trial of early detection of breast cancer, and to the project committee for permission to refer to these figures in this paper. I should also like to thank Dr Alexander, together with Dr M. M. Roberts, Dr A. E. Kirkpatrick and other members of that committee, for a number of helpful comments.

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Varicography in the management of primary varicose veins

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ABSTRACT

Forty-nine legs in 41 patients with primary varicose veins were investigated by varicography, (direct injection of varicose veins with contrast medium). Additional features not found at clinical examination, such as reduplication of the long saphenous vein, unusual terminations of the short saphenous vein and incompetent perforating veins, were found in over 50% of the legs examined. It is suggested that varicography should be carried out in patients with primary varicose veins in whom the clinical assessment is not conclusive

Generally the clinical assessment, including tourniquet tests and Doppler ultrasound, of primary (untreated) varicose veins presents no problem. The extent of the varicosities, their connections to either the long or short saphenous venous systems and any incompetent perforating veins can usually be established. However, in some patients the information so obtained is inadequate for appropriate management. These clinical difficulties arise because varicose veins do not affect the long and short saphenous veins uniformly. Sometimes the main trunks alone are affected and in others only the tributaries are varicose In a few cases both the long and short saphenous veins are involved. In extensive varicose veins, because of overlap of the long and short saphenous territories, it can be difficult to be certain which system is involved or whether both are affected. Incompetent perforating veins, particularly in the mid-thigh, and incompetent gastrocnemius veins are often impossible to diagnose clinically and even in the calf some may be missed. Anatomical variations such as reduplication of the long saphenous veins and unusual termination of the short saphenous vein can only be shown by phlebography.

In this paper we compare the findings on varicography (direct injection of the varicose veins with contrast medium) with the initial clinical diagnosis and indicate the way in which varicography may help in diagnosis and management.

MATERIAL AND METHODS

Forty-nine legs in 41 patients with primary varicose veins were assessed clinically and subjected to varicography. There were 30 women and 11 men, aged 20–66 years, mean 40 years Varicography was performed by our standard technique (Lea Thomas & Posniak, 1985), which involves direct injection of varicose veins with low-osmolality contrast medium, in this series iopamidol 300, to outline the veins and their connections.

RESULTS

Varicosities communicated with the long saphenous vein in 37 limbs (76%); in 22 of these (45%) the main long saphenous vein was varicose and in 15 limbs (31%) it was normal. Reduplication of the long saphenous vein was present in 14 varicograms (29%); of these all the channels were normal in eight limbs (16%) and one channel was varicose in six (12%). Varicose accessory long saphenous veins were shown in four limbs (8%) and a dilated, mid-thigh perforating vein in two limbs (4%).

In 16 limbs (33%) varicosities communicated with a short saphenous vein, the main vein being varicose in 12 legs (24%) and normal in four (8%). In five limbs (10%) varices connected with both the long and short saphenous veins. In three (6%) of the legs, incompetent-looking calf perforating veins were seen, and in three limbs (6%) varices connected with varicose gastrocnemius veins. In two of the 12 limbs (17%) in which varicose short saphenous veins were shown, the termination was not at the common site. In one limb

TABLE I

VARICOSITIES COMMUNICATING WITH THE LONG SAPHENOUS VEIN

	No of legs
Varicosities connecting with the LSV*	37
Main LSV varicose	22
Main LSV normal	15
Reduplication of LSV	14
All channels normal	8
One channel varicose	6
Varicose accessory LSV	4
Varicose mid-thigh perforator	2

*LSV = long saphenous vein

TABLE II

VARICOSITIES COMMUNICATING WITH THE SHORT SAPHENOUS VEIN

	No. of legs
Varicosities connecting with SSV*	16
Main SSV varicose	12
Main SSV normal	4
High termination of SSV	2

*SSV = Short saphenous vein.

(2%) a persistent lateral marginal vein of the leg was demonstrated in a patient later found to have Klippel Trenaunay syndrome.

No complications from varicography were encountered in this study. The results of the varicograms are summarised in Tables I, II and III and the additional features not obtained by clinical examination are shown in Table IV.

Discussion

Varicography has been used to demonstrate varicose veins and their connections for a number of years (Dow, 1952; Gullmo, 1956; May & Nissl, 1972; Doran & Barkat, 1981; de Fays et al, 1982) but it is only since the introduction of non-thrombogenic contrast media (Albrechtsson & Olsson, 1976) that the technique has become really safe (Lea Thomas & Briggs, 1984; Lea Thomas & Posniak, 1985).

It can be seen from Table IV that additional features were obtained by varicography not found clinically in over 50% of the cases. This additional information is

TABLE III

Varicosities communicating with incompetent perforating veins below the knee

	No. of legs
Incompetent calf perforating veins	3
Incompetent gastrocnemius veins	3

TABLE IV

Additional features demonstrated by varicography (not suspected clinically)

	No. of legs
Varicose LSV	1
Varicose accessory LSV	4
Reduplication of LSV	14
Incompetent mid-thigh perforating vein	1
Varicose SSV	6
High termination of SSV	2
Incompetent gastrocnemius vein	3
Incompetent calf perforating vein	2
Klippel Trenaunay syndrome diagnosed	1

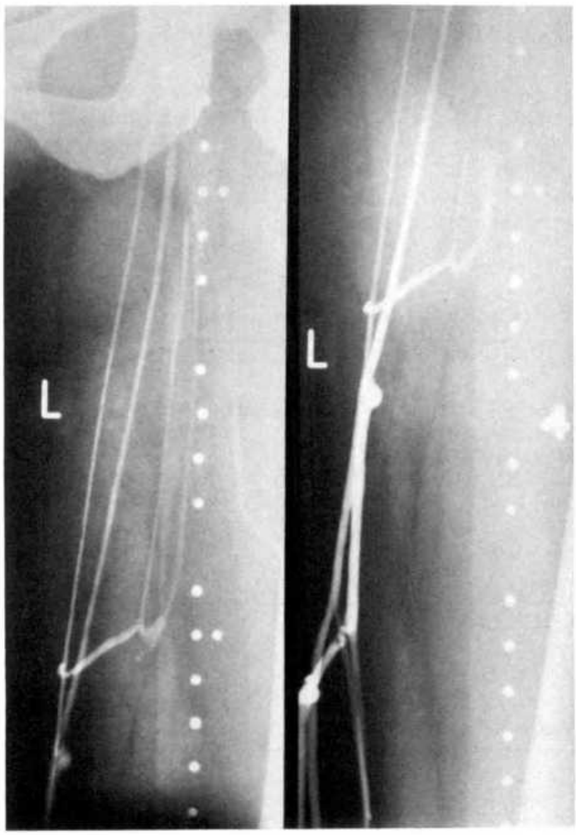


Fig. 1.

In this varicogram the long saphenous vein has multiple channels. This is important information if surgery is being considered.

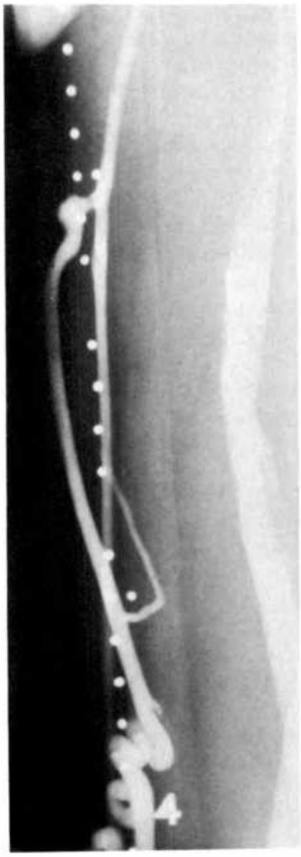


Fig. 2.

The long saphenous vein in this leg shows partial reduplication. Only the varicose channel needs to be ablated, preserving the normal one for future bypass surgery.

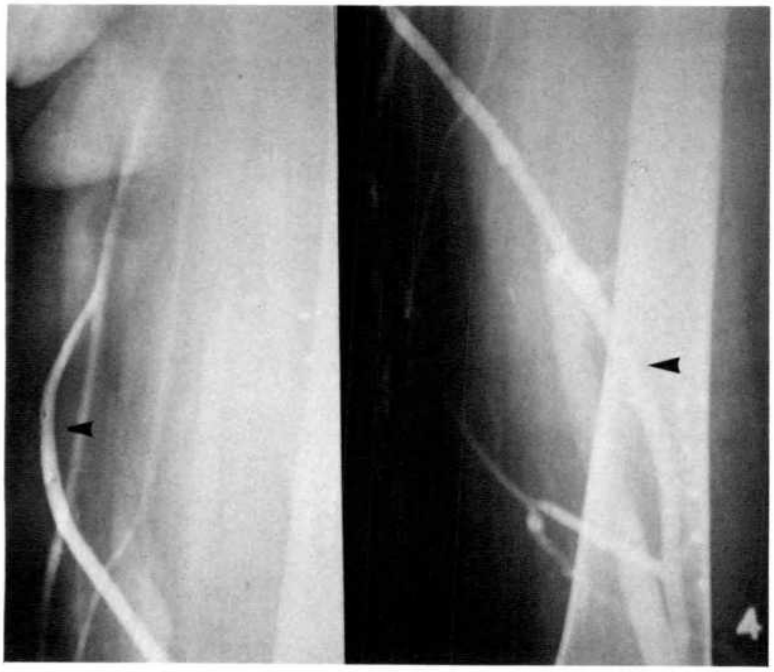


FIG. 3.

Varicose veins injected in the calf show that the main saphenous vein is reduplicated and normal and there is a medial accessory saphenous vein (arrows) which is a little varicose. Stripping of the main vein alone, leaving the accessory vein intact, would not eradicate the patient's calf varicosity.

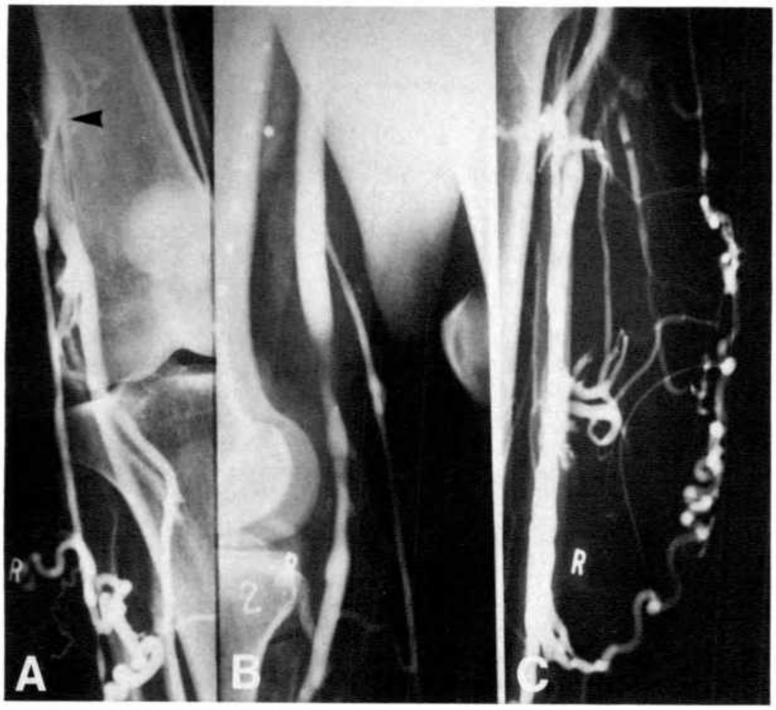


FIG. 4.

This varicogram shows an unusually high termination of the short saphenous vein (arrow). This affects the surgical approach for ligation. In the right-hand panel varicose veins can be seen in the calf connecting with a virtually normal main short saphenous vein. (A) Antero-posterior, (B) and (C) lateral.

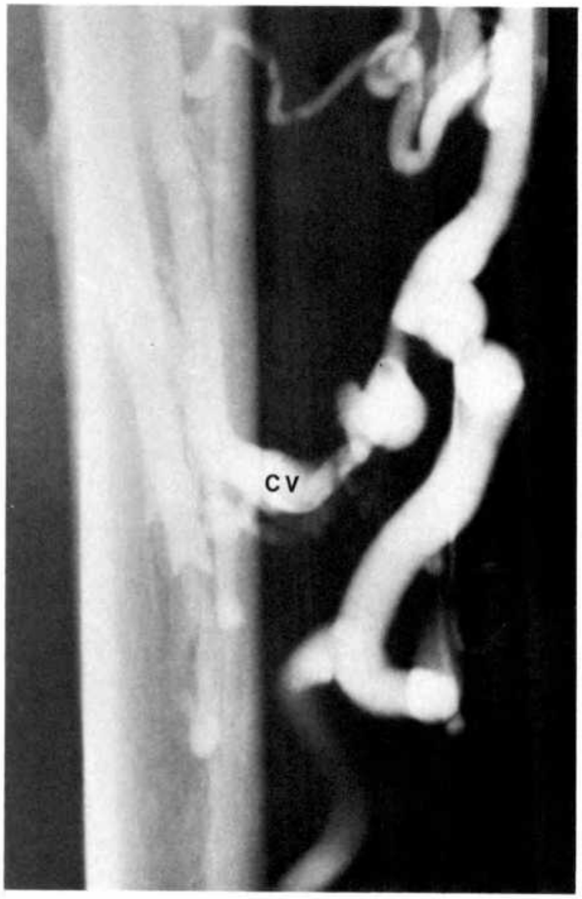


FIG. 5.

This varicogram shows a very large communicating vein (CV) filling from varicose veins and joining a posterior tibial vein. The direction of blood flow cannot be used as a criterion of incompetence but a perforating vein of this size can be assumed to be incompetent.

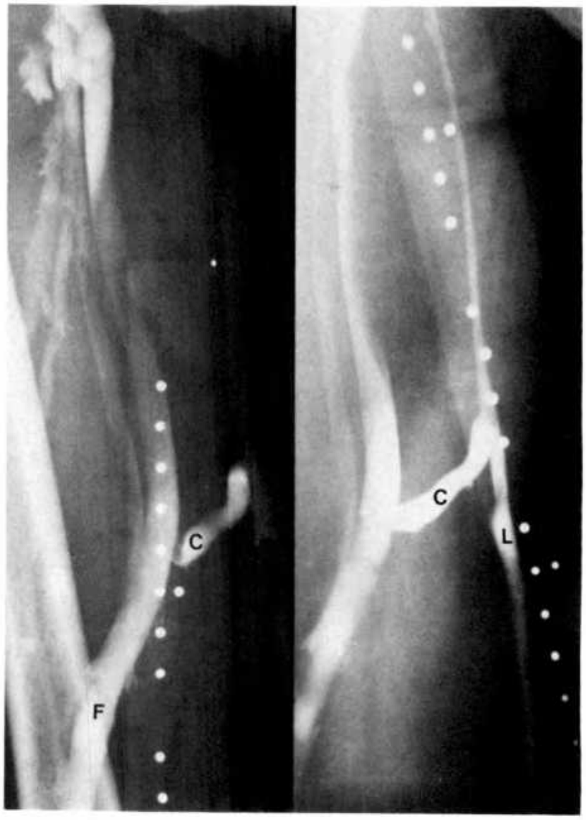


FIG. 6.

There is a dilated, valveless communicating vein in Hunter's canal (C) connecting the long saphenous vein (L) with the superficial femoral vein (F). This vein is almost certainly incompetent and if not ligated, along with ablation of the long saphenous vein, varicose veins are likely to recur.

often important in management. If tributaries of the saphenous veins alone are varicose and the main trunks normal, local avulsions or sclerosis may be all that is required.

It is important to preserve the long saphenous vein if at all possible, in case it is needed for bypass surgery. Reduplication of the long saphenous vein is common, occurring in almost one-third of the legs in this series, and if not known about beforehand could result in failure to ablate a varicose channel or, alternatively, unnecessary removal of a normal one (Figs 1, 2).

Rarely, confusion arises clinically as to which of the two saphenous systems is varicose and may result in incorrect treatment.

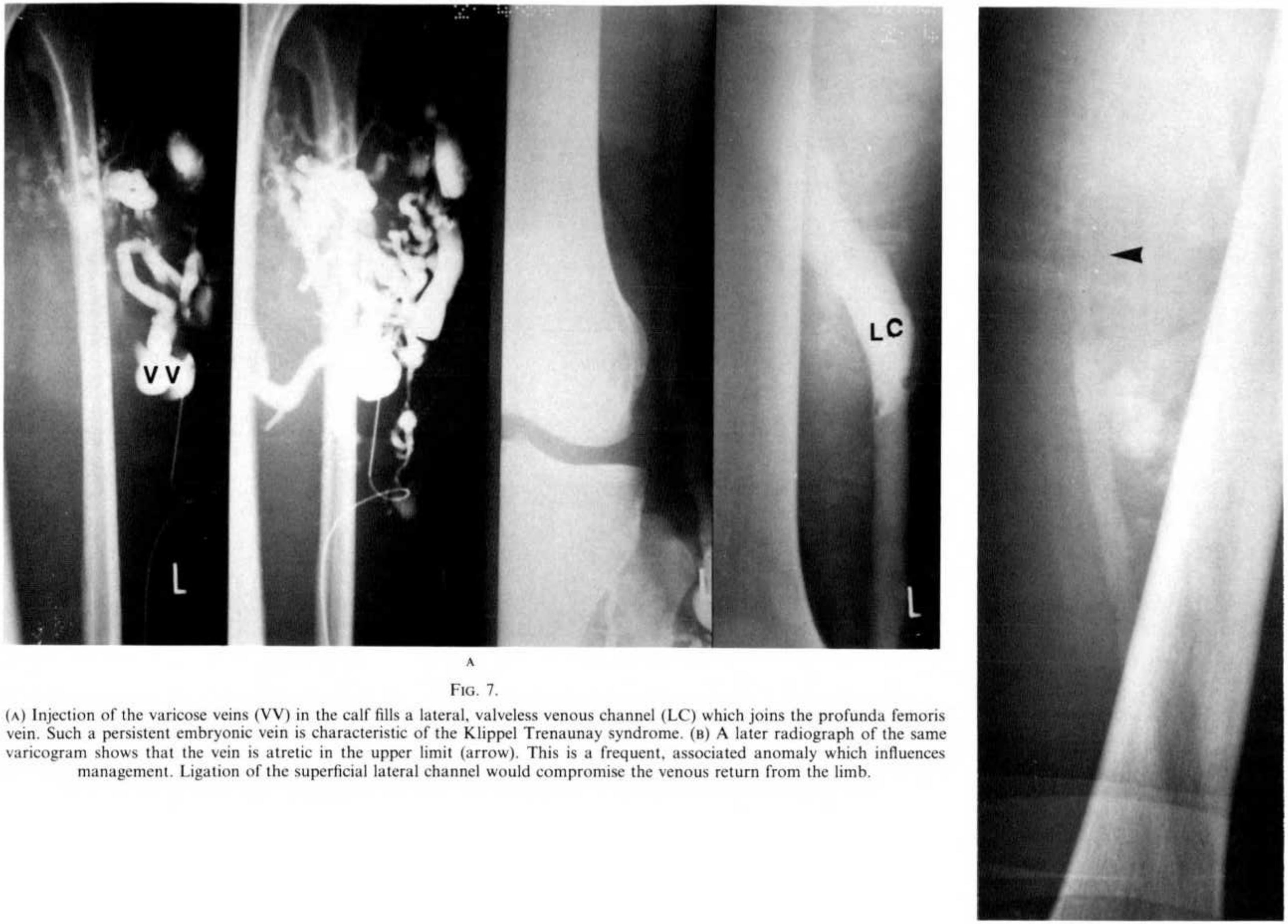
Accessory long saphenous veins occasionally occur and varicose veins may connect with these veins exclusively or with an accessory vein and the main long saphenous vein (Fig. 3).

Usually the short saphenous vein terminates in the popliteal fossa a few cm above the knee joint, but in almost one half of patients it terminates at a higher or lower level (Fig. 4). In this study 12 varicose short saphenous veins were demonstrated and of these 17% terminated at unusual sites. Unless flush ligation of the short saphenous vein is performed, recurrence is likely (Hobbs, 1980).

Incompetent perforating veins are not commonly found in primary varicose veins but, if present, do influence management. These may be in the calf, the gastrocnemius muscles or in the thigh (Figs 5, 6).

One of our patients was diagnosed by varicography as having the rare Klippel Trenaunay syndrome, which was not suspected clinically (Fig. 7).

In conclusion, this study has shown that varicography gives additional information relevant to management not obtainable or not appreciated by



A

B

FIG. 7.

(A) Injection of the varicose veins (VV) in the calf fills a lateral, valveless venous channel (LC) which joins the profunda femoris vein. Such a persistent embryonic vein is characteristic of the Klippel Trenaunay syndrome. (B) A later radiograph of the same varicogram shows that the vein is atretic in the upper limit (arrow). This is a frequent, associated anomaly which influences management. Ligation of the superficial lateral channel would compromise the venous return from the limb.

clinical assessment alone in nearly 70% of legs. We suggest that varicography should be performed in any patient in whom there are doubtful features which might affect treatment.

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Reproducibility of spin lattice relaxation time (T_1) measurement using an 0.08 tesla MD 800 magnetic resonance imager

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ABSTRACT

The reproducibility of T_1 measurements using an MD 800 magnetic resonance imager operating at 0.08 T (3.4 MHz) has been assessed by repeated imaging over a 15-week period of a phantom containing six copper-sulphate solutions of different dilutions. The standard pulse sequence for this scanner with an inversion time of 200 ms and a repetition time of 1 s was used. Reproducibility was excellent for the lower T_1 range (<350 ms), but greater variability was observed at higher T_1 values (>490 ms). A linear relationship between T_1 and temperature has been demonstrated and a method for standardising T_1 values obtained at different temperatures is described.

In-vivo measurement of spin lattice relaxation time (T_1) is helpful in differentiating between normal and abnormal tissues. It is important to ensure that measurements are reproducible, as a preliminary to establishing accurate normal ranges of T_1 for different tissues. To assess this, repeated measurements of a T_1 phantom have been made using the MD 800 imager.

METHOD

Ninety T_1 images of a phantom were obtained over 70 days between August 14 and November 27, 1985.

The phantom consisted of six plastic bottles held in a foam-rubber block which also held a standard mercury thermometer (R.S. Components Ltd). The bottles were 6 cm long and 4 cm in cross-sectional diameter. Each contained a different concentration of copper sulphate in distilled water. The phantom was kept in a standard position in the scanning room and fluctuations in temperature reflected changes in the ambient room temperature (16–23°C). The temperature was recorded immediately before scanning.

The phantom was positioned in the same orientation in the scanner on each occasion. A transverse section through the midpoint of the long axis of the bottles was selected in order to avoid partial-volume effects, thereby creating circular images of the six solutions. The slice thickness was 16 mm when the phantom was imaged in the body coil and 12 mm when it was imaged in the head coil.

The standard imaging procedure for the MD 800 0.08 T resistive magnetic resonance imager was used. This employs alternating saturation-recovery and inversion-recovery sequences with a repetition time (TR) of 1 s and an inversion time (TI) of 200 ms. From the data collected, the machine produces a calculated T_1 image (Eastwood, 1984). The T_1 of each solution was measured by placing a region-of-interest cursor centrally over the circular image of that solution. When the phantom was imaged in the body coil, the area measured was 4.04 cm^2 (33 pixels each measuring 3.5 mm × 3.5 mm). When the phantom was imaged in the head coil, the area measured was 4.84 cm^2 (121 pixels each measuring 2 mm × 2 mm).

RESULTS

Individual T_1 and temperature measurements together with linear regression lines for each bottle are shown in Fig. 1. The correlation coefficients for temperature and T_1 for each bottle are given in Table I. It can be seen from Fig. 1 that the regression lines are not parallel, but that the slope is lowest for the liquid of lowest T_1 and highest for the liquid of highest T_1. This increase in slope with T_1 is systematic. In Fig. 2 the slopes of the regression lines for each bottle (from Fig. 1) are plotted against the T_1 values at 20°C. The correlation coefficient for this relationship is very high ($r = 0.9998$). The regression line in Fig. 2 can be used to derive a relationship (see Appendix) between temperature, T_1 and equivalent T_1 values at 20°C as follows:

$$T_1(20) = \frac{85 \times T_1(t) - 31.8(t-20)}{52.8 + 1.61 \times t} \qquad (1)$$

where $T_1(20)$ is the T_1 value corrected to 20°C, t is the measured temperature and $T_1(t)$ is the measured T_1 at temperature t.

All measurements were corrected to 20°C, by applying Equation (1), to assess the reproducibility of T_1 measurements on different occasions independent of changes in temperature. The mean and standard deviation of these corrected T_1 measurements for each copper-sulphate solution are shown in Table II. The standard deviations of the T_1 measurements were less

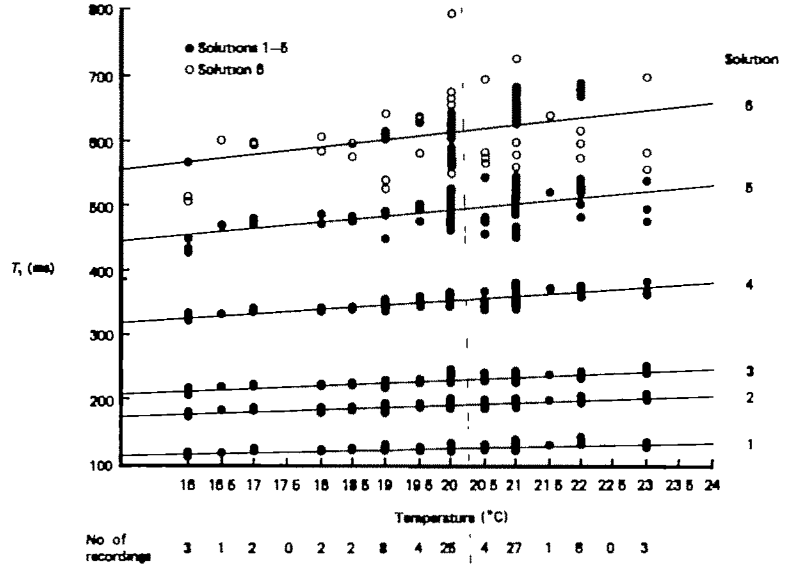

FIG. 1.

Temperature vs T_1 value for the six copper-sulphate solutions.

than 2% of the mean corrected T_1 values for the four solutions with T_1 between 127 ms and 355 ms. For the two solutions with T_1 greater than 490 ms, the standard deviations of T_1 were greater than 4% of the mean T_1.

T_1 values for copper-sulphate solutions 1–4 were examined further to assess the overall reproducibility of T_1 measurements in the lower T_1 range. The 90 T_1 values for each solution were expressed as percentages of the mean for that solution. On any particular study occasion these calculated values for the four solutions were, to an extent, either raised or lowered in concert (Kendall's concordance coefficient = 0.68, $p < 0.001$). The four percentage values for each occasion were then averaged. This average measures the extent to which T_1 readings are elevated or lowered on that occasion. The standard deviation of the 90 averages derived in this way was 1.2%. There was no detectable trend towards higher or lower values during the course of the study period.

TABLE I

CORRELATION COEFFICIENTS BETWEEN TEMPERATURE AND SPIN LATTICE RELAXATION TIME (T_1) FOR SIX COPPER-SULPHATE SOLUTIONS

Solution	Correlation coefficient
1	0.89
2	0.93
3	0.92
4	0.84
5	0.54
6	0.34

DISCUSSION

This study shows that there was excellent reproducibility (over a 15-week period) of T_1 measurements of liquids with T_1 values between 127 ms and 355 ms (at 20°C). The standard deviations of measurements on each copper-sulphate solution in this range were less than 2% of the mean T_1 values after correction for temperature.

The variability between T_1 measurements made on different occasions is best assessed by examining the mean percentage values derived from the T_1 values of copper-sulphate solutions 1–4. As the standard deviation of these values was 1.2%, differences of up to 5%

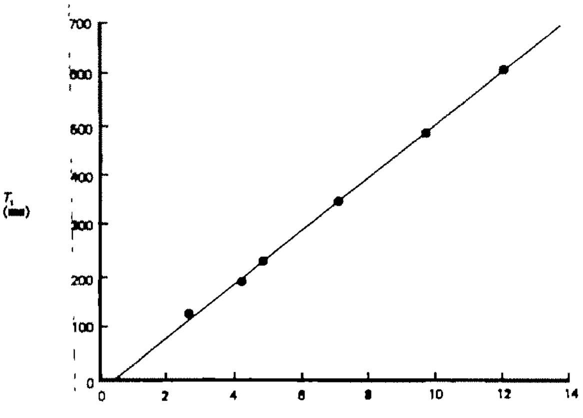

FIG. 2

Relationship of slopes of regression lines to T_1 readings at 20°C.

TABLE II

T_1 VALUES FOR THE SIX COPPER-SULPHATE SOLUTIONS CORRECTED TO 20°C

Solution	Mean T_1 (ms)	Standard deviation (ms)	Standard deviation as a percentage of mean T_1
1	126.7	2 0	1.6
2	194.0	2.3	1.2
3	232.8	2.9	1.3
4	355.0	6.4	1.8
5	493.3	21.5	4.4
6	613.6	47.8	7.8

fall within the conventionally accepted 95% probability limits (= ±2 standard deviations). Thus, differences in T_1 measurements of up to 5% may occur because of machine variation. Conversely, differences in T_1 measurements made on different occasions which are greater than 5% are unlikely to be because of machine variability. This degree of variability in the lower T_1 range is acceptable as it is small in comparison with the expected differences between T_1 values for normal and pathological tissues *in vivo* and *in vitro* (Hutchison & Smith, 1983). Furthermore, with this low percentage variability there is little to be gained by applying a correction factor for machine variability based on a daily phantom assessment. However, it is clearly important to continue daily phantom assessments to check that the machine is functioning within the limits established by this study.

The results indicate that for T_1 values above 490 ms there is greater variability in the measured T_1 values. It is known that the accuracy of T_1 measurement using this type of scanner is less good for samples with T_1 values which are not short compared with the repetition time used (Redpath, 1982). A pulse sequence with a longer repetition time would be expected to improve the accuracy of such measurements. Further studies are required to assess whether this would also improve the reproducibility of T_1 measurements made on different occasions.

This study has demonstrated a linear relationship between T_1 and temperature for the six copper-sulphate solutions. This may appear to conflict with the results from studies of biological tissues, reviewed by Bottomley et al (1984), in which T_1 has been shown to be linearly related to the inverse of absolute temperature. However, in the temperature range studied (16–23°C) a graph of temperature versus the inverse of absolute temperature closely approaches a straight line. Thus, any linear relationship found between T_1 and temperature also implies a linear relationship with the increase of absolute temperature. From the data in this study either relationship is equally valid. For the purposes of calculating a temperature correction factor, the simpler relationship (T_1 and temperature) was therefore chosen.

A temperature correction factor for each individual liquid could have been derived from the slopes of the individual regression lines in Fig. 1. However, as these lines are not parallel, no simple factor can be used for accurate correction of all liquids.

A general equation for temperature correction was therefore derived and applied in this study (see Appendix). Although the constants used in Equation (1) are probably unique to this scanner and should be determined independently for other scanners, the form of this equation is likely to have general applicability.

ACKNOWLEDGMENTS

We are grateful to the Joint Board of Research at St Bartholomew's Hospital and to the Jameel Research Fund for providing financial support. We thank Jane Ashby for secretarial assistance.

APPENDIX

The T_1 of any liquid increases with temperature. As demonstrated by Fig. 1 this relationship is linear, and is thus described by an equation of the form:

$$T_1 = i + st \tag{2}$$

where t is the temperature, T_1 the measured T_1 value at this temperature, i is the intercept of the line on the T_1 axis at $t = 0$, and s is the slope of the line. The slopes of the regression lines, s, in Equation (2) are themselves related by another regression line, for any particular temperature, *e.g.* 20°C, as shown in Fig. 2. Thus,

$$T_1(20) = a_1 + b_1 s \tag{3}$$

where $a_1 = -19\ 7$ and $b_1 = 52.8$ from Fig. 2. The intercepts, i, are related in a similar way:

$$T_1(20) = a_2 + b_2 i \tag{4}$$

where $a_2 = 12.1$ and $b_2 = 1.61$ Eliminating $T_1(20)$ from Equations (3) and (4) and solving for s,

$$s = \frac{a_2 - a_1 + b_2 i}{b_1}$$

Substituting for s in Equation (2) and solving for i and s:

$$i = \frac{b_1 T_1 - t(a_2 - a_1)}{b_1 + b_2 t}$$

$$s = \frac{b_2 T_1 + (a_2 - a_1)}{b_1 + b_2 t} \tag{5}$$

i.e. given any pair of values T_1 and t, Equation (2), describing the relationship over the whole range of temperatures, is uniquely determined by Equation (5).

Suppose we wish to correct for such a pair of values of $T_1(t)$ to the corrected T_1 reading at 20°C $T_1(20)$. Clearly, $T_1(20) = i + 20s$, and hence, using Equation (5).

$$T_1(20) = \frac{T_1(b_1 + 20b_2) + (a_2 - a_1)(20 - t)}{b_1 + b_2 t}.$$

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Measurement of radiation dose to the thyroid using positron emission tomography

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ABSTRACT

Measurements of the functioning volume of thyroid tissue have been made in 22 patients undergoing radioiodine therapy for thyrotoxicosis, using a prototype multiwire proportional counter positron camera. Tomographic images were produced of the distribution of ^{124}I in the thyroid. Functioning volumes were found to be in the range 21–79 cm^3 with volume errors of the order of $\pm 4\%$ to $\pm 14\%$. Radioiodine uptake varied from 28% to 98%. Using a value of 6 days for the effective half-life of radioiodine in hyperactive thyroids, radiation doses from a standard therapy administration of 75 MBq of ^{131}I varied from 11 to 48 Gy (compared with a recommended 50–70 Gy). In five cases PET imaging showed a non-uniform distribution of radioiodine in thyroids thought to have uniform uptake from conventional pinhole scintigraphy.

Measurements of the functioning volume of thyroid tissue enable the radiation dose given to the tissue during radioiodine therapy to be estimated. The effective treatment of diseases of the thyroid is directly related to the radiation dose achieved during radionuclide therapy. Since the functioning volume of the thyroid will generally be different from the anatomical volume, this can only be determined by radionuclide imaging techniques. Accurate measurements depend upon the inherent spatial resolution of the detector involved. Tomographic imaging is necessary to determine the intra-thyroid distribution of the radioisotope. In this paper the measurement of functioning thyroid volumes is achieved using a prototype multiwire proportional chamber positron camera. A simple model has been developed to determine the volume of the thyroid, and a measurement of the uptake and the effective half-life of the radionuclide in the thyroid are then sufficient to enable radiation dosimetry to be carried out.

VOLUME DETERMINATION TECHNIQUE

The determination of functioning volume is hampered by several physical difficulties but in particular by the classic problem of determining the edge of a distribution in the presence of background noise and the effects of finite spatial resolution. The simplest technique for volume measurement is to sum all volume elements (voxels) with a reconstructed count greater than some pre-set or threshold value. This technique is valid provided the structure of noise and spatial resolution remains relatively constant between studies. By using the phantoms of known volume, it was possible, firstly, to determine the variation of measured volume (V) with count threshold (T), and secondly, to test the appropriate algorithms determined by a simple model. This model (Webb et al, 1985) would be applicable if the thyroid were spherical in shape and the radionuclide were uniformly distributed within the organ. Considering Fig. 1, which shows a segment of a spherical distribution of radioactivity, a small change in the count threshold δT is related to the corresponding small change in linear dimension, δx, included in the volume, via the relationship

$$\delta x = -k_1 \delta T \qquad (1)$$

Hence since the curved area of the volume element is proportional to the square of the radius, the relationship between V and T becomes

$$\delta V = -k_2 V^{2/3} \delta T \qquad (2)$$

where $k_2 = 4.836\, k_1$.

In the limit as $\delta T \rightarrow 0$

$$-V^{-2/3} \mathrm{d}V/\mathrm{d}T = k_2 \qquad (3)$$

Hence, the prediction here is that the estimated volume V of the organ found at a threshold T is proportional to T^3.

No predictions are made for threshold values outside the organ volume. However, if statistical noise is considered to be the only other major contribution to the image, the counts in voxels outside the volume of the organ should have a normal distribution. This implies that raising the threshold on an image containing only statistical noise would give rise to a volume/threshold relationship of:

$$V \sim (1 - \mathrm{erf}(T)) \qquad (4)$$

where erf(T) is the integral of the normal distribution of frequencies. Hence, assuming the total counts in the

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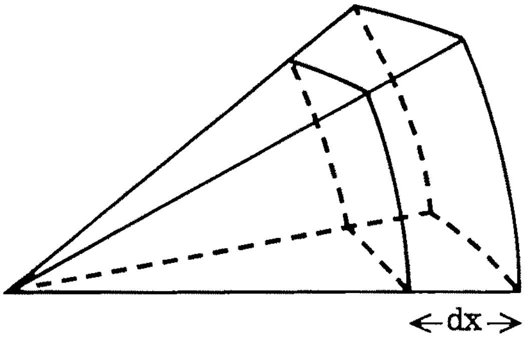


FIG. 1.

Segment of a spherical distribution of radioactivity.

image of the organ are considerably greater than the background noise, there should be a discontinuity in the relationship between V and T close to the value of T corresponding to the correct physical volume of the organ.

These predictions are clearly approximations and we have tested the results here using phantom and patient data.

DOSIMETRY

The mass of the thyroid can be calculated from the measured gland volume by assuming that the organ tissue density is unity. The absorbed dose to the organ (D), using the MIRD approach (Loevinger & Berman, 1968) is given by:

$$D = A/m\, \Sigma \Delta_i\, \phi_i \qquad (5)$$

where

Δ_i = equilibrium dose constant for the i'th radiation type

ϕ_i = absorbed fraction for the i'th radiation type absorbed in the thyroid

m = thyroid mass

A = time integrated activity within the thyroid

The value of A is given by

$$A = QU\, T_{\frac{1}{2}}/\ln 2 \qquad (6)$$

where

Q = activity administered to the patient

U = fractional thyroid uptake at 24 h (assumed to be at its maximum)

$T_{\frac{1}{2}}$ = effective half-life of radioiodine in the thyroid

In calculating the radiation dose to the thyroid from ^{131}I we assume the following parameter values.

$\Delta_{\text{electron}} = 2.8 \times 10^{-14}$ kg Gy/Bq s

$\Delta_{\text{photon}} = 4.8 \times 10^{-14}$ kg Gy/Bq s

$\phi_{\text{electron}} = 1.0$

$\phi_{\text{photon}} = 0.032$

$T_{\frac{1}{2}} = 6$ d (Harbert & Rocha, 1984; O'Connor et al, 1979)

MATERIALS AND METHODS

The prototype positron camera system has been extensively described elsewhere (Bateman et al, 1984). Briefly, the detectors have a sensitive area of 30×30 cm^2 and allow imaging throughout a sensitive volume of $20 \times 20 \times 20$ cm^3. The chambers are positioned on either side of the patient, who sits between them on a chair which can be positioned in eight different angular orientations at 22.5° intervals. The axis of rotation of the chair is perpendicular to the line joining the detector centres and parallel to the vertical axis of each detector. Rotation of the patient is necessary because the prototype detectors were not designed for mechanical movement. The configuration is equivalent to rotating the chambers through eight discrete orientations about a stationary patient to provide eight contiguous views. The chambers were operated in coincidence with a resolving time of 10–15 ns and approximately 400 000 events were acquired per study.

Twenty-two patients were chosen from those visiting the thyroid clinic at the Royal Marsden Hospital at Sutton who were undergoing radioiodine therapy for hyperthyroidism. Instead of the usual oral dose of 75 MBq of ^{131}I, the patients received an equivalent mixed dose of 55 MBq of ^{131}I and 25 MBq of ^{124}I. Images with the positron camera were taken 24 h after ingestion. The thyroid uptake was determined using a calibrated scintillation counter and planar scintigraphy was carried out using a Nuclear Chicago HP37 gamma camera and a pinhole collimator. Informed consent was sought from each patient before the study.

The PET reconstruction technique is a two-stage process of back projection followed by deconvolution (Clack et al, 1984) of a theoretical point-source response function to produce a $64 \times 64 \times 64$ volume image, with a pixel size of 3 mm. Image noise suppression was achieved using a Hanning window with a frequency cut-off $c = 0.32$ pixel^{-1}. The spatial resolution in deconvoluted images depends on the degree of frequency windowing. It is relatively insensitive to position within the field of view and was typically of the order of 10 mm with this filter. The reconstructed data could be displayed as transaxial, sagittal and coronal sections as well as a three-dimensional shaded contour image (Ott et al, 1986).

Two thyroid phantoms each consisting of two perspex cylinders joined by a small tube and filled with ^{68}Ga were used to determine the parameters required for volume measurements. The volumes of these two phantoms were 72.5 cm^3 and 26 cm^3. Thyroid volume measurements for both phantoms and patients were made using the threshold technique previously described. Estimates of local variations of radiation dose within the thyroid were made by the addition of a region of interest to isolate the nodule or area being evaluated.

No attempt was made to measure the effective half-life of the radioiodine in the thyroid of each patient as

TABLE I

COMPARISON OF RESULTS OF PLANAR SCINTIGRAPHY AND PET IMAGING OF THE THYROID

	Planar		
	Uniform uptake	Non-uniform uptake	Total
PET			
Uniform uptake	13	0	13
Non-uniform uptake	5	4	9
Total	18	4	22

this required either pre-evaluation with a test dose or sequential daily measurement of thyroid radioactivity during therapy. As most patients were outpatients, neither of these procedures was easy to perform in this present study.

RESULTS

Imaging

Table I compares the results of PET imaging of the thyroid with those of the planar imaging. Out of the 22 patients imaged, planar scintigraphy showed 18 to have uniform uptake and 4 multinodular or non-uniform uptake. The PET scan, however, determined that of the 18 patients with apparent uniform uptake, five had non-uniform uptake. There were no cases where multinodular or non-uniform uptake was detected by planar imaging and not by PET.

Thyroid volume measurements

In Fig. 2 we see the variation of estimated volume (V) with percentage count threshold (T) for the two thyroid phantoms. Both show a change in slope close to the point corresponding to the actual volume of the phantoms at a value of T between 40 and 45%. Figure 3 shows the variation of V with T for two patients, one with uniform radionuclide uptake (A) and a second with non-uniform radionuclide uptake (B). Again, these data indicate a change of slope at a threshold value in the region 40–45%. Figures 4A,B illustrate typical 3 mm coronal sections through the thyroids of these two patients. Sample profiles through these images (Figs 4C,D) show the effects of finite resolution. Figure 5 is a

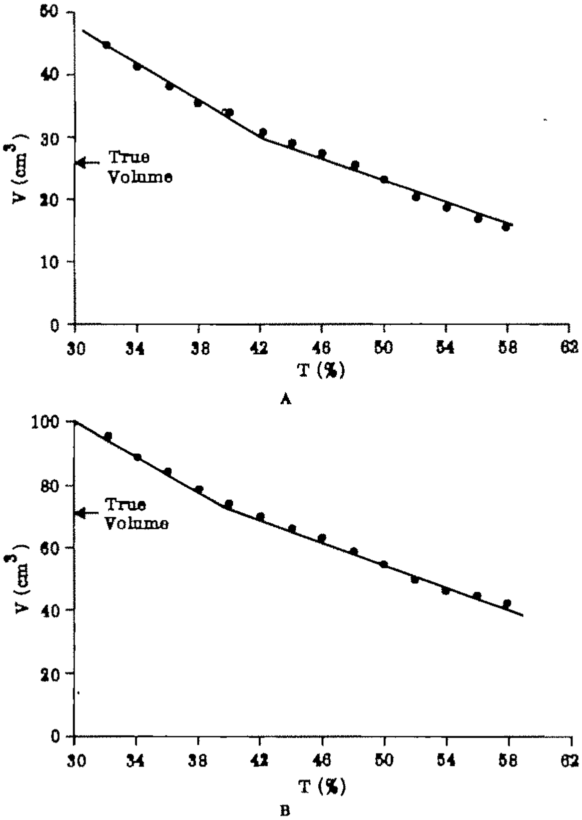


FIG. 2.

V vs T for (A) the small, 26 cm³ thyroid phantom and (B) the large, 72.5 cm³ thyroid phantom.

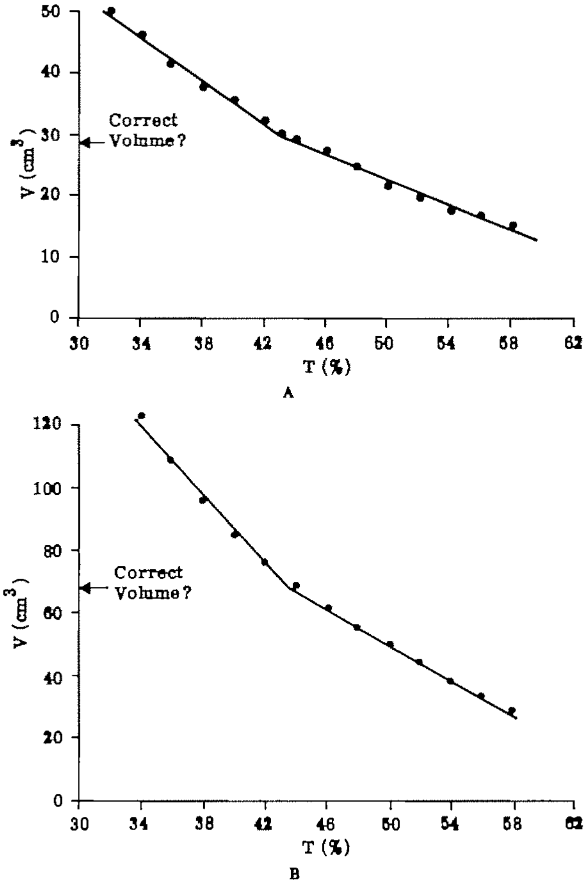


FIG. 3.

V vs T for a patient with (A) uniform radionuclide uptake and (B) multinodular or non-uniform radionuclide uptake in the thyroid.

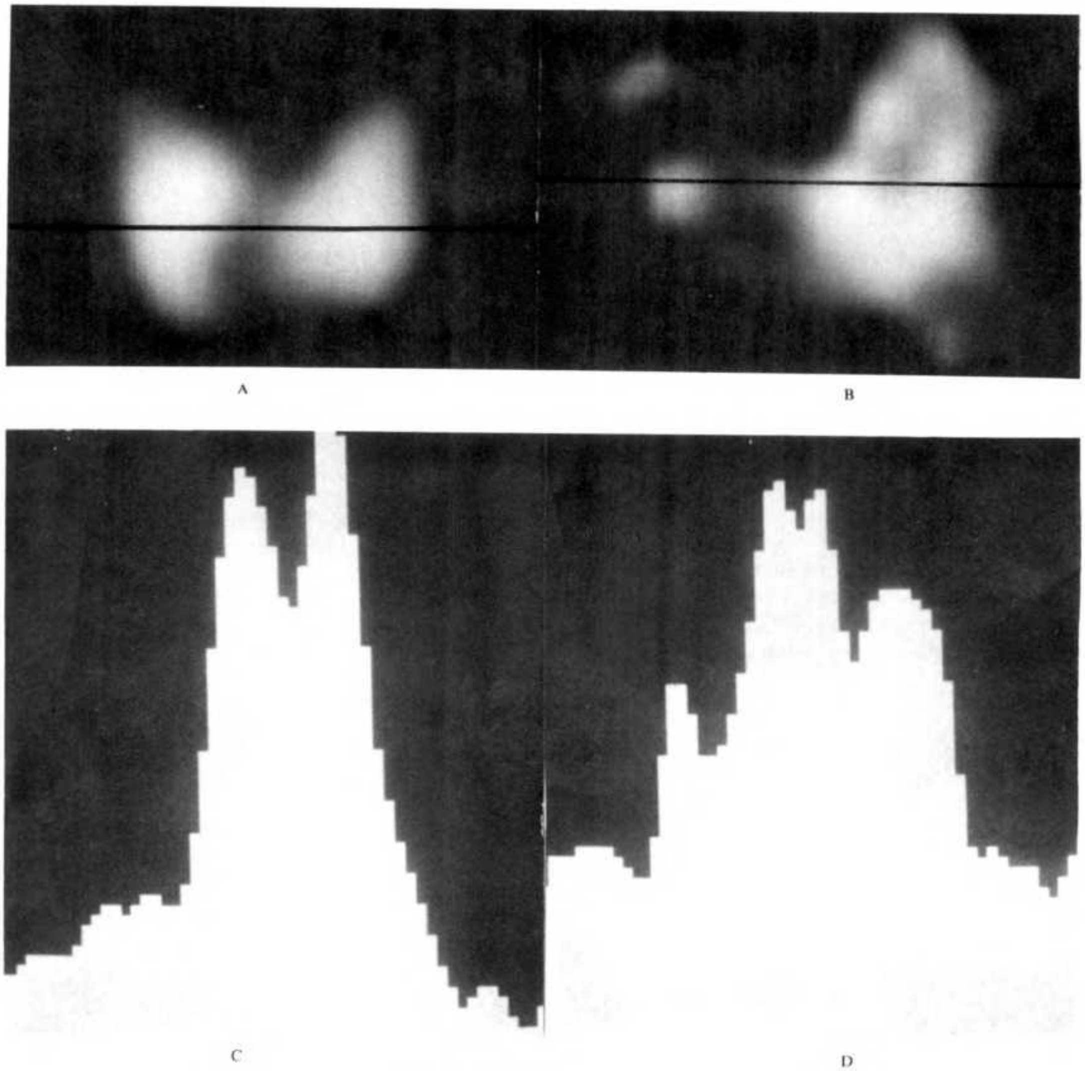


FIG. 4.

Coronal sections (3 mm thick) through the thyroids of the patients in Fig. 3, with (A) uniform radionuclide uptake and (B) non-uniform radionuclide uptake. (C) and (D) show horizontal profiles through the two sections shown in (A) and (B).

plot of $-V^{-2/3}\mathrm{d}V/\mathrm{d}T$ as a function of T for the two phantoms and four patients. These data show that for the two phantoms the relationship in Equation (3) is approximately correct and the value of k_2 is ~ 0.13. The data for the two patients whose radioiodine uptake in the thyroid was uniform are entirely consistent with that obtained from the phantoms. The two other patients shown had non-uniform radioiodine uptake and in these cases the relationship is invalid at small values of threshold. At thresholds above 40–45% the relationship holds approximately, although with a large value for the constant, k_2, of ~ 0.23.

The existence of the point of inflexion in the curve of V against T at a threshold value T_1 giving a volume V_1 close to that of the true volume has been confirmed, using a range of phantoms with volumes in the range 1–250 ml. The value of V_1 was determined for all patients imaged and found to be in the range 21–79 ml. For some patient thyroid measurements, several points of inflexion were observed and here the most likely value of T_1 was chosen after visual inspection of the images produced when the threshold was set at each inflexion point. Figure 6 shows the relationship between the thyroid volume V_1 and $-\mathrm{d}V/\mathrm{d}T$ at this volume for each patient. We can see from this that the power law relationship described in Equation (3) holds well for all patient thyroid volume measurements, although the values of the constants differ from those predicted by

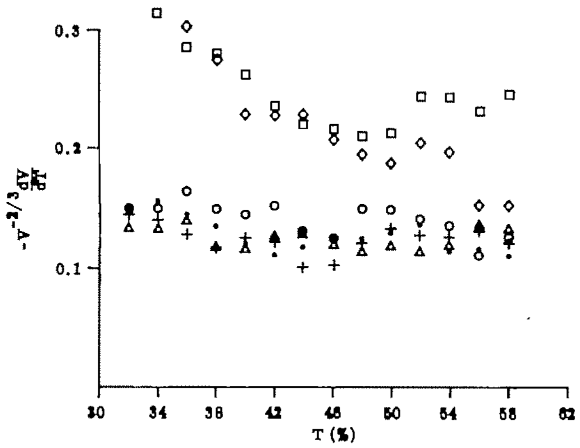


FIG. 5

$-V^{-2/3}dV/dT$ vs T for the two thyroid phantoms and four patients. ● Large thyroid phantom, + small thyroid phantom, ○, △ uniform thyroid uptake, □, ◇ non-uniform thyroid uptake.

the simple model. The relationship between thyroid uptake (U) and volume (V_I) is shown in Fig. 7, indicating no correlation between these measurements.

A mean threshold, T_M, 44.1±1.1% was determined for patients with a uniform uptake, and 43.6±2.2% for patients with non-uniform uptake (Table II). The errors on the measurements of the volume were obtained from the value of dV/dT at the point of inflexion. The overall percentage error in the volume for thyroids with uniform uptake is thus estimated to be ±4–5% (±0.9–2.2 cm^3) and for thyroids with non-uniform uptake is ±8–14% (±4.0–12.4 cm^3).

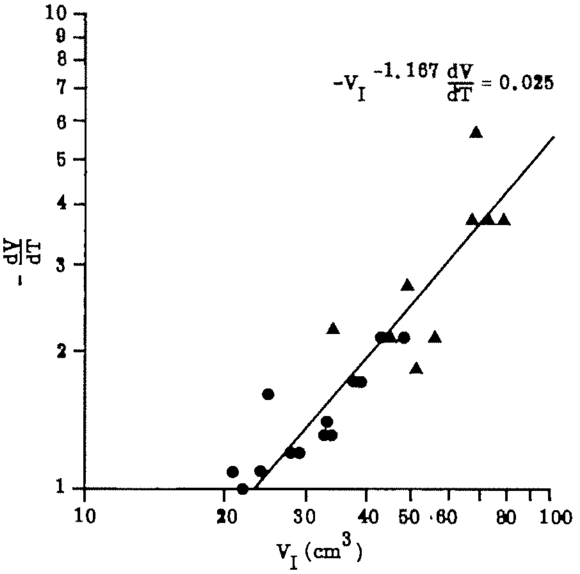


FIG. 6

dV/dT vs V at T_I for all patient thyroids. ● uniform thyroid uptake, ▲ non-uniform thyroid uptake (logarithmic scale).

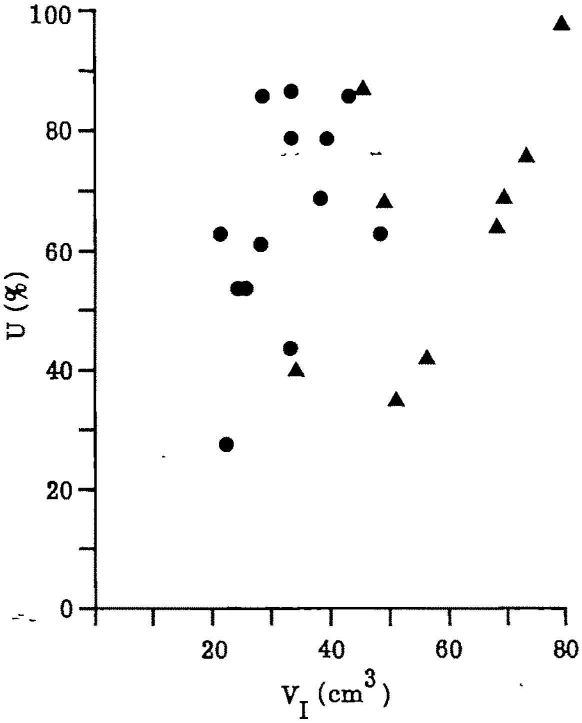


FIG. 7.

Iodine uptake in the thyroid (U) vs thyroid volume (V_I). ● uniform thyroid uptake, ▲ non-uniform thyroid uptake.

Radiation dosimetry

Tables IIA and IIB show the results of the thyroid radiation dose estimates made for each patient assuming the standard activity of 75 MBq of ^{131}I has been administered in each case. Also shown are values for the radionuclide uptake (U) at 24 h as a percentage of administered dose, the values of T_I, the volumes V_I at T_I, values of V_M at T_M and values of dV/dT at T_I.

Estimates of the intrathyroid radiation dose have been made for two patients showing multinodular or non-uniform uptake. The thyroid of patient No. 16 consisted of two normal anatomical lobes plus a third nodule situated inferior to the isthmus. The thyroid of patient No. 17 showed the radionuclide distribution to be uniform on planar scintigraphy, but was clearly non-uniform in the PET images. The whole thyroid and intrathyroid doses are shown in Table III. It can be seen from these data that the variation of radiation dose for patient No. 16 was ±20% and for patient No. 17 was ±25%.

TABLE II

VALUES OF RADIONUCLIDE UPTAKE (U), THRESHOLD AT POINT OF INFLEXION (T_I), FUNCTIONING VOLUME AT T_I (V_I), FUNCTIONING VOLUME AT T_M(V_M), dV/dT AT T_I AND RADIATION DOSE (D), FOR PATIENT THYROIDS WITH:

(A) Uniform radionuclide uptake

Patient	U(%)	T_I(%)	V_I(cm³)	V_M(cm³)	dV/dT	D(Gy)
1	86	45	43	46	2.1	30
2	87	44	33	34	1.4	41
3	63	44	48	49	2.1	21
4	63	44	21	22	1.1	46
5	28	43	22	22	0.9	21
6	79	42	39	36	1.7	36
7	79	43	33	32	1.3	40
8	86	45	28	29	1.2	48
9	54	46	25	29	1.6	30
10	69	45	38	40	1.7	28
11	61	44	28	28	1.2	35
12	44	43	34	33	1.3	22
13	54	45	24	25	1.1	35

$T_M = 44.1 \pm 1.1\%$

(B) Non-uniform radionuclide uptake

Patient	U(%)	T_I(%)	V_I(cm³)	V_M(cm³)	dV/dT	D(Gy)
14	64	44	68	69	3.7	13
15	98	40	79	69	3.7	23
16	68	42	49	44	2.7	25
17	76	43	73	69	3.7	18
18	42	42	56	53	2.1	13
19	87	43	45	45	2.1	31
20	35	45	51	53	1.8	11
21	71	48	69	85	5.7	13
22	40	45	34	36	2.2	18

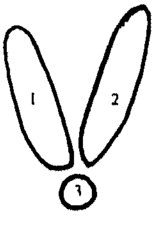
$T_M = 43.6 \pm 2.2\%$

TABLE III

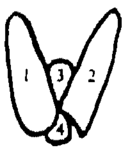
ESTIMATED INTRA-THYROID RADIATION DOSES (GY)

Patient No.	Whole gland	Region 1	Region 2	Region 3	Region 4
16	25	29.5	23.5	19	—
17	18	22	19	17.5	26

Patient No. 16



Patient No. 17



DISCUSSION

The variation of the estimated volume (V) with percentage count threshold (T) generally shows a discontinuity at values of T close to 44%. For the two thyroid phantoms the discontinuities occur at values of V very close to the actual measured volume and this has been confirmed subsequently, using a greater range of phantoms. These results are in agreement with the predictions made earlier in the paper. For the thyroid glands where the PET images show a uniform uptake of the radionuclide, the change in slope of the curve of V against T is usually clearly seen, but for those glands where uptake appears non-uniform, it is sometimes difficult to identify the exact position of the discontinuity. This is almost certainly caused by statistical variations in the data at T values close to T_I. However, as shown in Tables IIA, B, there is a relatively small range of values of T_I and it was possible to use a mean value T_M for the threshold to obtain values of the thyroid volume. This value of 44% is very close to the findings of Tauxe et al (1982) in SPECT who quote 45% for cylinders of volume less than 1000 cm³. The standard error on T_M is small because of the measurement precision of the positron camera so that the range of errors on the volume are ±0.9–2.2 cm³ for thyroids with uniform uptake. Multinodularity or non-uniformity of radionuclide distribution in the gland increases the estimated error on volume to ±4.0–12.4 cm³ in these cases. Even in the worst case, this leads to an error of only ±14% in the thyroid volume The data in Fig. 5 show that the assumption made for the relationship between linear dimension and threshold is only approximately true. Figure 6, however, indicates that the relationship between V_I and dV/dT is better described by the form:

$$-V_I{}^{-1.167}\,\mathrm{d}V/\mathrm{d}T = 0.0252 \tag{7}$$

The difference between Equations (3) and (7) shows the expected inaccuracy of the model. Instead of the linear edge profile predicted by Equation (1), it is seen that the data (Fig. 6) are consistent with an edge profile which is non-linear and is more accurately given by.

$$\mathrm{d}x = -k_1\,\mathrm{d}T x^{3/2} \tag{8}$$

It should be noted that all thyroid volume measurements made were consistent with Equation (7) and that the substitution of a more complex three-dimensional object, such as a pair of spheroids, would not affect the underlying relationship shown here and only the values of the constants would change.

It can be seen from Table II that the range of thyroid radiation doses is estimated to be 11–48 Gy. This is to be compared with levels estimated from an administered activity based on gland size and uptake (Harbert & Rocha, 1984). With recommended activity levels of 2–3 MBq/g, radiation doses of 50–70 Gy to the thyroid were achieved. The variation in radiation dose achieved in our study is related to both the range of uptake levels in the thyroid (28–98%) and the functioning volume of the organ (21–79 cm^3) and bears out the need for the administration of a fixed dose per gram of thyroid. The errors in these radiation dose measurements are a consequence of volume, activity and half-life uncertainties. Volume measurement errors are in the range of ±4 to ±14% and errors in the measurement of thyroid radionuclide uptake are ±10%. As we have not measured the effective half-life of the radioiodine in the thyroid of each patient, we have chosen to use the value of 6 d quoted by Harbert and Rocha (1984) and O'Connor et al (1979). Hence, no overall error can be estimated for the radiation dose measurements presented here. However, it is clear from this study that administration of a standard 75 MBq dose of ^{131}I to this set of patients could lead to an enormous range in therapeutic effect irrespective of effective half-life and the uniformity of the radionuclide distribution in the thyroid. If the maximum possible effective half-life of 8 d is used this increases the estimated range of radiation doses to 15–64 Gy which still indicates that many patients have received inadequate radiotherapy.

Figure 7 shows that there is no apparent correlation between the size of the organ and the percentage uptake of radioiodine; nor is this uptake correlated with whether the radionuclide distribution is uniform or not. However, in general, the volume, and hence the mass, of the thyroids showing non-uniform uptake is larger than of those with uniform uptake.

In the case of non-uniform thyroid uptake, there will be a consequent inhomogeneity in the distribution of the radiation dose within the thyroid and this leads to further uncertainties in the radiation dose achieved. However, these appear to be at a significantly lower level than uncertainties caused by variation in thyroid volume and uptake.

We have not considered here the effects of other treatment, the use of thyroid drugs or the microscopic variations between thyroid tumours which may lead to differing radiation sensitivities and, hence, variable radiotherapy response.

Follow-up of all patients in this study is now in progress to determine if the subsequent treatment/results correlate with the findings reported here.

Conclusions

By using a high-resolution positron camera it has been possible to measure the functioning thyroid volume to an accuracy of ±4–14%. The radiation doses to the thyroid from 75 MBq of ^{131}I were calculated to vary from ~ 11–48 Gy in the 22 patients studied here, indicating that an unsatisfactory therapeutic effect will be obtained in many cases unless the administered activity is adjusted. Additionally, the images from PET show that the radionuclide distribution in some thyroid glands is non-uniform when the conventional imaging indicates otherwise. Clearly a more quantitative approach to radioiodine therapy for thyrotoxicosis is required. This should include a tailoring of the administered dose of ^{131}I to match the measured functioning mass and the uptake of the gland under treatment.

Acknowledgments

We would like to acknowledge the help of the radiographers of the Nuclear Medicine Department and Dr C. Harmer and his staff in the Thyroid Unit of the Royal Marsden Hospital.

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Book reviews

Roentgen Signs in Diagnostic Imaging Vol. 2. Appendicular Skeleton. By Isadore Meschan, pp. xxviii + 507, 1985 (W.B Saunders, Philadelphia), £85.00.
ISBN 0–7216–6303–6

This is the second of three volumes of the revised versions of Meschan's *Analysis of Roentgen Signs in General Radiology* which was published originally in 1973. The first volume of the set covered the abdomen and has been reviewed previously.* There are to be four volumes in all, one on the skull and spine, the other on the chest.

This volume covers the appendicular skeleton. The introductory chapter includes definitions of the descriptive terms used in bone radiology, an outline of radiographic projections used, and a simple resumé of the physical principles of computed tomography (CT). This is followed by a succinct account of bone physiology and calcium metabolism. the chapter on fractures and their healing provides much useful information for trainees in radiology, particularly during their early days of casualty film reporting and includes diagrams of various joint prostheses and the complications which may be seen following joint replacement. Subsequent chapters are arranged to cover conditions which cause either increased or reduced bone density, and congenital and developmental anomalies. This leads to some repetition of both text and diagrams, but this is inevitable given that each chapter is intended to stand as an independent unit.

The emphasis of the book is again on conventional radiographic techniques, but the last chapter is devoted to CT and includes good quality, annotated xeroradiographs of anatomical cross-sections through the arm and leg showing the normal soft-tissue anatomy of the limbs. The radiographic illustrations are profuse and generally of high quality and some CT sections are included. Good and effective use has been made of numerous line diagrams. There are many lists and tables, giving the causes or differential diagnoses of a variety of clinical and radiological features. These are clearly set out and are particularly useful for rapid reference. The book contains a wealth of basic information, and includes descriptions of the assessment of bone age and the application of quantitative CT to bone-mass measurement. Selected relevant and pertinent references are given at the end of each chapter to guide the reader to more detailed study

This would make an excellent bench book for trainee radiologists and especially during their introduction to skeletal radiology Although only half the size of the first, this volume is almost twice the price, presumably reflecting inflation and increase in publishing costs, but the aims and high standard set in the first volume have been maintained The book is still good value and I would recommend its purchase for any departmental library used by trainees in radiology. Junior members of other clinical disciplines, such as orthopaedics and rheumatology, may also find much relevant information.

J. E. ADAMS

*1985. *British Journal of Radiology, 58,* 146.

Roentgen Signs in Diagnostic Imaging Vol. 3. By Isadore Meschan, pp 630, 1985 (W. B. Saunders, Philadelphia), £83.00.
ISBN 0–7216–6304–4

Isadore Meschan has been a familiar name in radiological publications for more than a quarter of a century. The present volume, third in an expanded sequel to an earlier work, has enlisted the help of four additional contributors. They have restricted themselves largely to plain radiographs and computed tomography (CT). Special procedures, nuclear medicine and ultrasound are omitted, and magnetic resonance imaging must await a future edition.

One of the book's strengths is that it brings together in one volume material and illustrations from a wide range of sources. It has more detailed anatomy and radiographic technique than comparable radiology textbooks. The anatomical diagrams are clear and extensively labelled (the section on the petrous temporal bone is particularly well done). Common pathology is covered crisply and lucidly.

The plain-radiograph reproductions are of a high standard, as are the CT scans of the spine though not all those of the brain. As with previous volumes, some illustrations have been duplicated (*e.g.* Fig 3–45 on p. 249 and Fig. 5–7 on p. 495), and two radiographs of a normal parotid sialogram on succeeding pages (pp. 359 and 361) is one too many.

The section on the spine, particularly on basic principles and pathology, is excellent. Detailed description of abnormalities on myelography is limited, as the authors prefer CT of the spine with low-dose contrast enhancement. Metrizamide is the favoured contrast medium and iopamidol gets only a brief mention.

There are extensive references, most of which are relevant, and up to date within the limits of the book's date of publication (1985). The text is easy to read, with only occasional errors, though the format adopted leads to some repetition.

Meschan says his book is for "students, residents and practitioners" and that is about right. It will be of most value to radiologists in training. Budding surgeons and rheumatologists will find something of use in it, and general radiologists will benefit from its presence in the library

GORDON EVISON

1987, *The British Journal of Radiology*, 60, 253–259 MARCH 1987

Strontium-89 therapy: strontium kinetics and dosimetry in two patients treated for metastasising osteosarcoma

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ABSTRACT

We report a study of strontium kinetics in two patients who received ^{89}Sr therapy for disseminated osteogenic sarcoma, together with estimates of absorbed dose to the principal metastases and to bone marrow. In neither patient did tumour uptake of strontium have a significant effect on whole-body retention. In one patient, whole-body strontium kinetics agreed closely with the ICRP standard model, while in the second, retention was extremely prolonged, probably due to hypertrophic osteoarthropathy. Strontium-85 scintigraphy, surface counting and high-resolution whole-body profiles agreed in showing that in both patients tumour turnover of strontium was very rapid, with a biological half-life of only a few days. Absorbed dose to tumour was found to be comparable in magnitude to the mean bone-marrow dose. We have no reason to believe that ^{89}Sr therapy was of clinical benefit to either patient.

Pecher (1942) was the first to report a possible therapeutic role for the beta-emitting radionuclide ^{89}Sr in the palliation of skeletal malignancy. Subsequent reports (Firusian et al, 1976; McEwan et al, 1986; Robinson, 1986) have encouraged the belief that ^{89}Sr administered at 1–2 MBq kg^{-1} bodyweight might prove beneficial in the management of metastatic bone disease with only minimal deleterious effect on haemopoiesis. Autoradiographic studies by Low-Beer, recalled by Brucer (1976), demonstrated the selective uptake of ^{89}Sr in osteoblastic areas surrounding osteogenic and Ewing's sarcoma, suggesting that ^{89}Sr therapy might also be of value in the palliation of disseminated osteosarcoma. Apart from a report by Mazabraud et al (1982) describing the use of ^{85}Sr kinetic studies to assist the classification of osteogenic sarcomas, little is known about strontium kinetics in patients with osteosarcoma, or about the absorbed dose to tumour that might be achieved following ^{89}Sr therapy. In this report we describe a study of strontium kinetics in two patients treated with ^{89}Sr for metastasising osteosarcoma at the Department of Nuclear Medicine, Southampton General Hospital. For each patient, estimates are made of the radiation dose delivered to the most prominent metastases demonstrated by ^{99}Tc^{m} MDP scintigraphy, and these are compared with the estimated mean dose to red marrow.

METHOD

Patients

Both patients were offered ^{89}Sr treatment after conventional cytotoxic therapy had proved unsuccessful. They were treated during the course of a clinical trial to evaluate ^{89}Sr therapy in patients with metastatic bone disease (Blake et al, 1986; McEwan et al, 1986).

Case 1

At the age of 19 years, a neoplasm, originally diagnosed as a chondroma, was excised from her left chest wall. Two years later a recurrence was found, and chest radiographs, a CT scan and ^{99}Tc^{m} MDP scintigraphy showed multiple pulmonary metastatic deposits in both lung fields. After a percutaneous lung biopsy, the diagnosis was revised to metastatic osteogenic sarcoma. Several courses of chemotherapy with methotrexate, cis-platinum and adriamycin were given with no response, and palliation with ^{89}Sr was offered. The anterior and posterior ^{99}Tc^{m} MDP images of the chest immediately before strontium therapy are shown in Figs 1A, B. Multiple soft-tissue metastases are seen in both lungs. The largest metastasis, located anteriorly in the left upper zone, was selected for a dosimetric study. A CT image through the centre of this metastasis is shown in Fig. 1C.

Case 2

An amputation of the right leg for osteogenic sarcoma of the femur was performed at the age of 17 years. A year later, a chest radiograph and a CT scan demonstrated lung metastases, which progressed rapidly despite chemotherapy with cis-platinum and adriamycin. Palliation with ^{89}Sr was given. The anterior and posterior ^{99}Tc^{m} MDP images of the chest immediately before strontium therapy are shown in Figs 1D, E. There was a large soft-tissue metastasis posteriorly in the right upper zone together with metastatic deposits in the sternum and right sixth rib. The bone images also showed intense diffuse uptake of ^{99}Tc^{m} MDP in the long bones associated with hypertrophic osteoarthropathy (HPOA). The right upper zone metastasis and deposit in the sternum were selected for dosimetric study.

Administration of radiostrontium

Both patients received a therapeutic dose of ^{89}Sr together with a tracer dose of ^{85}Sr for the kinetic studies. Details of the emissions, half-lives and specific activities of the two radionuclides are given in Table I. Case 1 received 92.5 MBq of ^{89}Sr (1.48 MBq kg^{-1} bodyweight) and 15 MBq of ^{85}Sr, and Case 2 received

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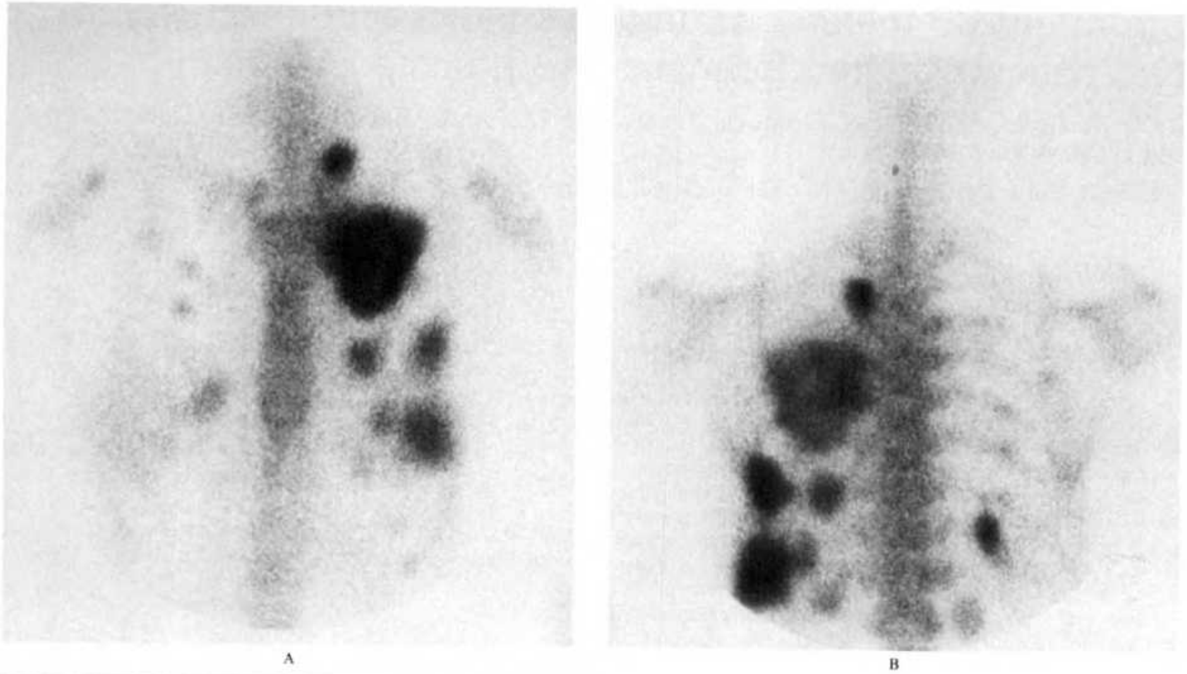

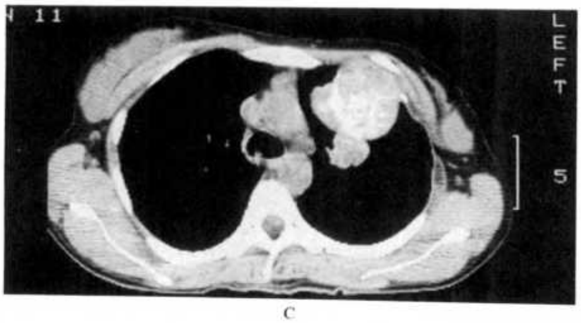

FIG. 1A, B, C. *Case 1.*

(A) and (B) are anterior and posterior ^{99}Tc^{m} MDP images of the chest showing multiple soft-tissue metastases. The most prominent lesion, located anteriorly in the left upper zone, was selected for dosimetric study. The CT image (W = 350) through the centre of this metastasis is shown in (C).

158 MBq of ^{89}Sr (2.96 MBq kg^{-1} bodyweight) and 40 MBq of ^{85}Sr. After measurement in an isotope assay calibrator, ^{89}Sr and ^{85}Sr were administered simultaneously via a peripheral vein with a constant infusion rate over a 1 min interval. No adverse reactions were observed.

Plasma and urine measurements

Case 1

Following strontium administration, blood samples from a different vein were drawn at 45 and 90 min, 3, 5 and 9 h, and 1, 2, 3, 4 and 7 days later. After centrifuging in a heparinised tube, two 1 ml aliquots of plasma from each blood sample were prepared for assay in an automatic gamma counter. Complete daily urine collections were made during the first week following treatment. Urine volumes were measured and two 1 ml aliquots prepared for assay from each collection. Plasma and urine samples were assayed against ^{85}Sr standards that had been measured in the isotope assay calibrator before dilution in 500 ml of distilled water. A correction was made for ^{89}Sr bremsstrahlung.

Case 2

Plasma and urine samples were similarly measured, but the period of study extended only over the 24 h following ^{89}Sr therapy.

In both patients, plasma and urine data were combined to measure the renal plasma clearance rate for strontium (Harrison et al, 1955). The renal path is the major route for normal strontium excretion (Harrison & Sutton, 1967).

Whole-body monitoring

A shadow shield whole-body counter (WBM) with adjustable collimators set 1 cm apart was used to monitor whole-body retention of ^{85}Sr and to obtain high-resolution head-to-feet profiles. Corrections for radioactive decay and small variations in WBM sensitivity were made by running through the WBM before every patient counting session a standard 10 kg phantom containing around 4 MBq of ^{85}Sr.

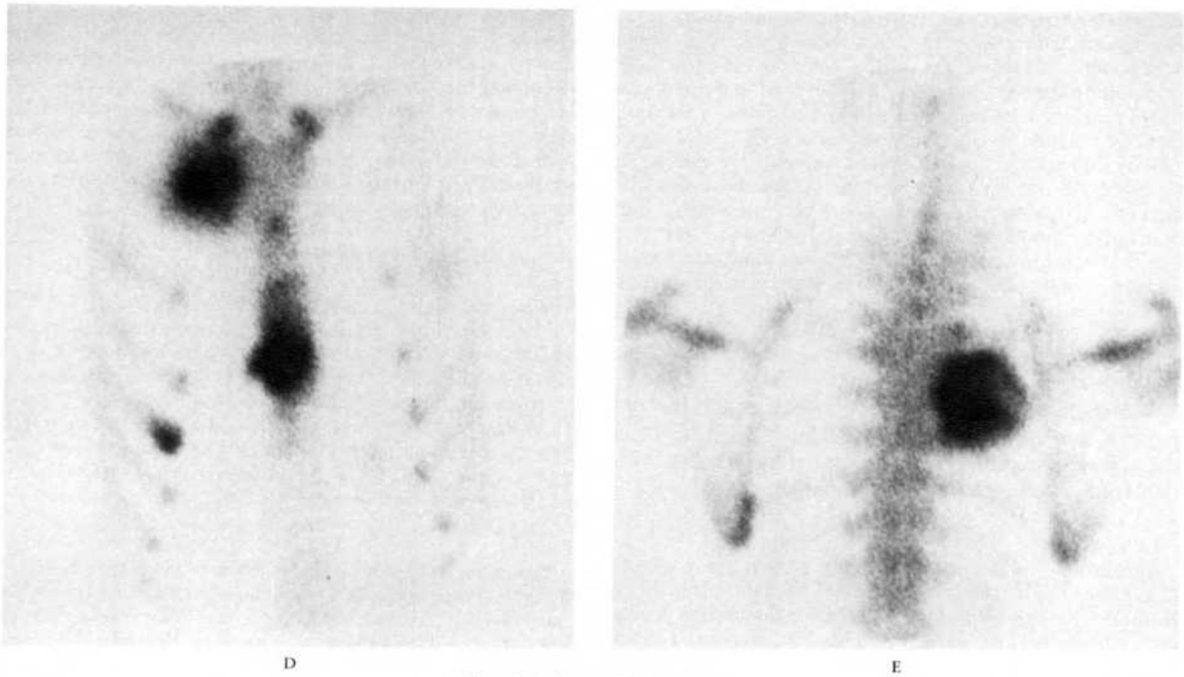

FIG. 1. (D) AND (E). *Case 2.*

A soft-tissue metastasis is located posteriorly in the right upper zone and bony metastases in the sternum and right sixth rib. The former were chosen for dosimetric study.

Case 1

The WBM measurements were made 15 min after strontium administration, daily during the first week, on 4 days during the second week and thereafter at intervals up to 3 months.

Case 2

Measurements were made at 15 min and 4 h following ^{89}Sr therapy, and then at 1, 2, 5 and 12 days later.

After subtraction of background and correction to the standard, all patient counts were normalised to the 15 min value to give percentage whole-body strontium retention. A printout of counts in 1 cm intervals for each whole-body profile measurement was kept for later analysis of strontium retention in selected regions of interest.

TABLE I

DETAILS OF THE EMISSIONS, HALF-LIVES AND SPECIFIC ACTIVITIES OF ^{89}Sr AND ^{85}Sr

	^{89}Sr	^{85}Sr
Transition	Beta minus (E_{max} = 1.46 MeV)	Electron capture
Gamma emission	(910 keV)	514 keV
Half-life	50.5 days	64.8 days
Specific activity	5 GBq/g	500 GBq/g

Abundance of the 910 keV gamma ray associated with the decay of ^{89}Y^m is 1×10^{-4}. Radiostrontium was administered as the chloride.

Surface counting and ^{85}*Sr scintigraphy*

Case 1

Strontium-85 retention in the large soft-tissue metastasis located anteriorly in the left upper zone (Fig. 1A) was monitored by surface counting on each occasion the patient attended for WBM counting. An external scintillation probe was used to measure the count rate over the tumour together with the counts over the symmetrical contralateral site free of disease. After correction for radioactive decay, the difference in count rate between the tumour and its control site was attributed to metastatic uptake. Phantom measurements were made, reproducing the counting geometry *in vivo* as accurately as possible to convert the surface counting results into strontium uptakes expressed as percentage of injected dose. The results were in good agreement with approximate estimates of tumour uptake made from the WBM profiles.

Case 2

At the time this patient was treated, a high-energy gamma camera collimator rated to 511 keV and suitable for imaging ^{85}Sr was available. On each occasion he attended for WBM counting, anterior and posterior scintigraphic images of the chest were recorded on a nuclear medicine computer system and used to monitor strontium uptake in the soft-tissue metastasis in the right upper zone and the bony metastasis in the sternum (Figs. 1D, E). Images of the left femur were also recorded to monitor uptake in cortical bone at a site affected by HPOA. The scintigraphic images were analysed by drawing appropriate regions of interest to define tumour counts above background. Corrections for radioactive decay and variations in gamma camera sensitivity were made using scintigraphic images of the WBM phantom. For the soft-tissue metastasis in the chest, anterior and posterior view tumour counts were combined with a transmission measurement through the body, using a point source of ^{85}Sr of known activity to determine tumour uptake corrected for attenuation by overlying tissue as a percentage of injected dose. This method of attenuation correction has previously been described for adrenocortical scintigraphy by Sudell et al (1985). For the sternal metastasis, the anterior view alone was used to measure tumour uptake without any correction for attenuation.

RESULTS

Whole-body strontium retention

Whole-body strontium retention curves for the two patients are shown on a log–log plot (Fig. 2) in which the normal retention function adopted by Marshall et al (1973) has been included for comparison.

Case 1

Whole-body retention followed the normal curve closely, falling to around 20% at 3 months. Metastatic uptake of strontium was apparent on the high-resolution WBM profiles only during the first week following ^{89}Sr therapy. Tumour uptake had a negligible effect on whole-body turnover.

Case 2

The whole-body retention curve was extremely flat, falling to around 84% at 12 days after ^{89}Sr therapy compared with a normal value of 30% at this time. Examination of the WBM profile for Day 12 showed that the strontium present was retained in the skeleton and, had the patient remained well enough for WBM counts to continue, we anticipate that the very flat retention curve would have continued (Blake et al, 1986). As with Case 1, tumour uptake of strontium was apparent on the profiles only during the first week following therapy. Unlike Case 1, however, there were major changes in strontium kinetics in the normal skeleton. Not only was retention very high, but the distribution of strontium in the skeleton was unusual, with very prominent uptake in cortical bone compared with the usual predominance of trabecular uptake. This latter feature correlated closely with the scintigraphic changes due to HPOA.

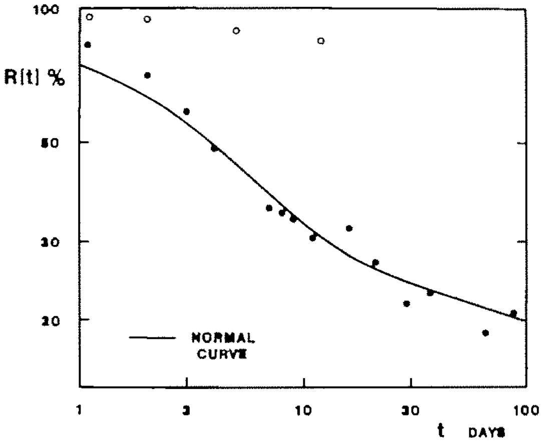

FIG. 2.

A log–log plot of whole-body strontium retention against time for the two patients reported in this study: ○ Case 2; ● Case 1. The high skeletal strontium uptake in Case 2 is probably due to hypertrophic osteoarthropathy associated with the patient's pulmonary metastases. The solid line is the normal whole-body retention function (Marshall et al, 1973).

Renal plasma clearance of strontium

Case 1

When the plasma curve and renal excretion data for ^{85}Sr were combined, the renal plasma clearance rate was found to be 7.6 l day^{-1}. The normal value adopted by Marshall et al (1973) was 8.3 l day^{-1}. In a group of five healthy adult men, Harrison and Sutton (1967) reported values between 8.1 and 15.4 l day^{-1}. A measurement of the 24 h creatinine clearance after the end of chemotherapy and before treatment with ^{89}Sr gave a value of 143 l day^{-1} (normal range 115–215 l day^{-1}). Renal strontium clearance in Case 1 was therefore normal.

Case 2

Strontium renal plasma clearance was found to be 1.5 l day^{-1}. A measurement of the 24 h creatinine clearance after the end of chemotherapy and before treatment with ^{89}Sr gave a value of 219 l day^{-1}. The low renal strontium clearance rate was therefore due to high renal tubular reabsorption. We speculate that this increase in tubular reabsorption was associated with the patient's HPOA, possibly mediated by an endocrine disturbance of calcium homeostasis. A similar phenomenon associated with sclerotic bone metastases has been reported in patients with disseminated carcinoma of the prostate (Urwin et al, 1986).

Tumour uptake curves

The results from surface counting, ^{85}Sr scintigraphy and examination of whole-body profiles were all consistent in showing that strontium turnover in the metastatic lesions was rapid, with biological half-lives for ^{89}Sr of a few days only.

Case 1

The ^{85}Sr uptake curve for the soft-tissue metastasis in the chest measured by surface counting is shown in Fig. 3A. Strontium turnover is rapid, the uptake falling to half its peak value in 6 days. There is a suggestion that the curve may be biphasic.

Case 2

The ^{85}Sr uptake curve for the soft-tissue metastasis in the chest measured by scintigraphy is shown in Fig. 3B. The curve is monoexponential up to Day 12 with a half-life of 3.6 days. Also shown (Fig. 3C) is the curve for the sternal metastasis, with a half-life of 11 days, and, in contrast, the curve for cortical bone in the femur, which is extremely flat.

DOSIMETRY

Tumour dosimetry

The measurements of tumour strontium kinetics described above permit estimates of absorbed dose using the following equation for beta-particle dosimetry:

$$D_T = 1.6 \times 10^{-10} U_T \mathrm{SEE}(T \leftarrow T) \text{ Gy} \qquad (1)$$

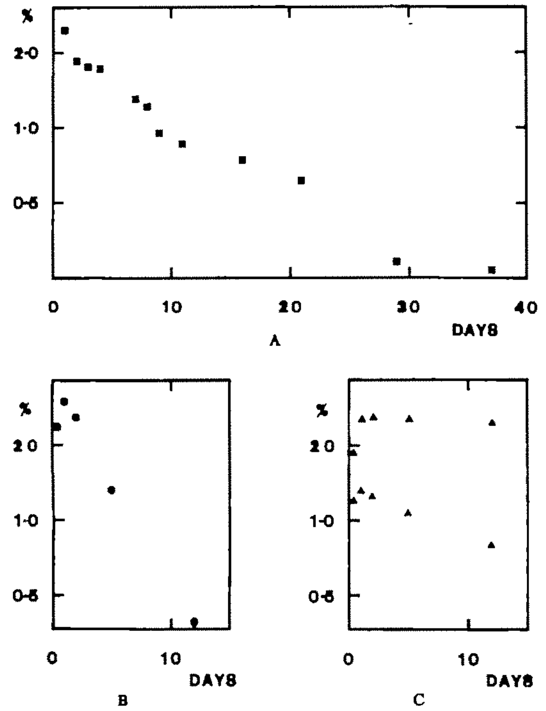

FIG. 3.

Log–linear plot of tumour strontium uptake expressed as a percentage of injected dose against time following strontium administration. (A) Left upper zone soft-tissue metastasis in Case 1. (B) Right upper zone soft-tissue metastasis in Case 2. (C) Case 2. ▲ Bony metastasis in the sternum. △ Uptake curve for an area of cortical bone in the proximal end of the left femur.

where D_T is the mean tumour dose, U_T the number of beta transformations occurring in the tumour for complete decay of ^{89}Sr, and SEE (T ← T) the specific effective energy for tumour. Equation 1 has been adapted from Equation 4.3 of ICRP Publication 30, Part 1 (ICRP, 1979). We may write:

$$U_T = A_0 \int_0^\infty f(t) e^{-t/\tau}\, dt \qquad (2)$$

where A_0 is the ^{89}Sr activity (Bq) initially administered to the patient, $f(t)$ the fractional tumour retention at time t (seconds) and τ the mean physical life of ^{89}Sr. We also write:

$$\mathrm{SEE}(T \leftarrow T) = \frac{\bar{E}_\beta \mathrm{AF}(T \leftarrow T)}{M_T} \quad \mathrm{MeV\,g^{-1}\,transformation^{-1}} \qquad (3)$$

where $\bar{E}_\beta = 0.583$ MeV is the mean beta-ray energy for ^{89}Sr (Cross et al, 1983), AF(T ← T) = 1.0 is the absorbed fraction for beta rays originating in the tumour and M_T the tumour mass (g).

Masses for the metastases whose strontium kinetics had been studied were estimated from tumour volumes measured from a CT study, performed close to the treatment date, using routine software provided by the manufacturer. The volumes obtained in this way were checked against volumes estimated from the linear dimensions of the tumours measured from anterior, posterior and lateral view ^{99}Tc^m MDP images recorded immediately before ^{89}Sr therapy (Fig. 1). Tumour mass was then obtained by assuming a density of 1.0 g cm^{-3} for the soft-tissue metastases and 2.0 g cm^{-3} for the bony metastasis, figures consistent with the Hounsfield numbers recorded on the CT studies. The values of A_0,

$$\int_0^\infty f(t)\, e^{-t/\tau}\, dt,\ M_T$$

and the value of D_T inferred from Equation (1) for the metastases studied are summarised in Table II.

Bone marrow dosimetry

Estimates of the mean absorbed dose to bone marrow for each patient were obtained as follows.

Case 1

Here the whole-body strontium kinetics agreed closely with the normal retention function of Marshall et al (1973) (Fig. 2). A quantitative measure of this agreement was obtained by

TABLE II

SUMMARY OF THE ESTIMATED ABSORBED DOSE TO THE PRINCIPAL METASTASES AND TO BONE MARROW FOLLOWING ^{89}Sr THERAPY

	A_0 (MBq)	$\int_0^\infty f(t)\, e^{-t/\tau}\, dt$ (s)	M_T (g)	D_T (cGy)
Case 1				
Soft-tissue metastasis (left upper zone)	92·5	22 600	90	220
Mean bone marrow dose	–	–	–	120
Case 2				
Soft-tissue metastasis (right upper zone)	158	12 500	110	170
Bony metastasis in sternum	158	18 200	65	410
Mean bone marrow dose	–	–	–	620

The absorbed dose to metastases was estimated from the initial ^{89}Sr activity administered to the patient (A_0), the time integral of the fractional tumour retention corrected for physical decay

$$\left(\int_0^\infty f(t)\, e^{-t/\tau}\, dt\right),$$

and the tumour mass (M_T) using Equations (1)–(3) in the text. Estimates of bone marrow dose were based on ICRP Publication 30 (ICRP, 1979).

comparing for the patient and the normal kinetic model the effective mean life T of ^{89}Sr in the body:

$$T = \int_0^\infty R(t)\, e^{-t/\tau}\, dt \qquad (4)$$

where $R(t)$ is the fractional whole-body retention and τ the physical mean life of ^{89}Sr. A value of T of 18.6 days was found for Case 1, compared with 19.0 days for the normal retention function. It was therefore assumed that a reasonably accurate estimate of bone marrow dose in this patient could be found by a calculation which combined the normal kinetic model with the ICRP model of bone dosimetry (ICRP, 1979). The resulting derivation of mean dose to red bone marrow following intravenous administration of ^{89}Sr is given in the Appendix to this paper The result obtained is 1.31 cGy MBq^{-1}, and this figure was used for the estimate of marrow dose given in Table II.

Case 2

Here the whole-body strontium retention was extremely high. From studies of patients with disseminated carcinoma of the prostate (Blake et al, 1986) with similar retention curves to this, we anticipate a power law extrapolation of the measured curve in Fig 2, which would lead to an effective mean life $T = 58$ days in Equation (4). This suggests that an approximate estimate of bone marrow dose can be obtained by assuming it to be around three times greater than that predicted by the ICRP model, giving the figure in Table II. However, this may be an overestimate, as a disproportionate part of the increased strontium retention was seen in cortical rather than trabecular bone, and ^{89}Sr in cortical bone makes a rather small contribution to mean marrow dose (ICRP, 1979)

As part of the clinical follow-up of each patient, regular blood cell counts were obtained. The results for white cell and platelet counts are summarised in Table III.

CONCLUSIONS

The figures for absorbed dose to metastases given in Table II can only be regarded as approximate estimates. However, it is impossible to avoid the conclusion that the tumour doses achieved were of the order of a few hundred centigray, rather than the few thousand centigray usually required for clinically effective radiotherapy, and that they were comparable to, and in Case 2 probably less than, the mean absorbed dose to bone marrow. This finding arises because, although the specific uptake of ^{89}Sr per gram of tissue was higher in metastases than in normal bone, biological turnover of strontium was much more rapid. This latter fact was demonstrated by ^{85}Sr scintigraphy, surface counting measurements and whole-body profiles, which all agreed in showing that strontium uptake in the tumours fell rapidly, reaching levels comparable with background within 1–2 weeks of ^{89}Sr therapy. For effective tumour doses to have been given in the face of this observation, initial tumour uptake of strontium would have to have been of the order of 10–30% of the injected dose. Such high uptakes were clearly excluded by the early WBM profiles, which were consistent with the direct measurements of tumour uptakes of 1–3% obtained from the surface counting and scintigraphic studies.

TABLE III

SUMMARY OF THE WHITE CELL AND PLATELET COUNTS FOUND IMMEDIATELY BEFORE ^{89}Sr THERAPY AND AT MONTHLY INTERVALS THEREAFTER

Time from therapy	Case 1		Case 2	
	White cell count 10^9/l	Platelet count 10^9/l	White cell count 10^9/l	Platelet count 10^9/l
Before	3.5	221	5.9	314
1 month	2.5	147	3.4	128
2 months	2.2	170	–	–
3 months	5.3	155	–	–

Case 2 was not well enough for follow-up to continue after the first month. The integrated mean bone marrow dose at 1 month after therapy was estimated to be 60 cGy for Case 1 and 220 cGy for Case 2.

There is no evidence that ^{89}Sr therapy was of clinical benefit to either patient. In Case 1, disease progression has been slower than anticipated and she remains well 18 months after strontium therapy despite progressive pulmonary metastases demonstrated by radiography. In Case 2, the disease was aggressive, and he died 2 months after therapy with no evidence that ^{89}Sr treatment altered the course of his illness.

ACKNOWLEDGMENTS

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APPENDIX

CALCULATION OF ABSORBED DOSE TO BONE MARROW

The mean absorbed dose to red bone marrow following intravenous administration of ^{89}Sr may be estimated on the basis of the ICRP dosimetric model for bone (ICRP, 1979) together with data from the ICRP model for normal strontium kinetics (Marshall et al, 1973 (also published as ICRP Publication 20)).

We start with the following equation adapted from Equation 7.1 of ICRP Publication 30, Part 1 (ICRP, 1979):

$$D_{RM} = 1.6 \times 10^{-10} \sum_{s} U_s \, \mathrm{SEE}(RM \leftarrow S) \ \mathrm{Gy} \qquad \text{(A1)}$$

where:

D_{RM} is the absorbed dose to red bone marrow (RM);

U_s is the number of nuclear transformations occurring in source organ S for complete decay of the nuclide;

$\mathrm{SEE}(RM \leftarrow S) = \dfrac{E_\beta \, \mathrm{AF}(RM \leftarrow S)}{M_{RM}}$ is the specific effective energy;

$E_\beta = 0.583$ MeV is the mean beta-ray energy of ^{89}Sr (Cross et al, 1983);

$M_{RM} = 1500$ g is the mass of active red bone marrow (ICRP, 1979);

$\mathrm{AF}(RM \leftarrow S)$ is the absorbed fraction in red marrow from nuclear transformations in S.

Red marrow is irradiated principally by ^{89}Sr in trabecular bone (TB), but there is a small contribution from cortical bone (CB). From Table 7.3 of ICRP Publication 30, Part 1 (ICRP, 1979):

$$\mathrm{AF}(RM \leftarrow TB) = 0.42$$
$$\mathrm{AF}(RM \leftarrow CB) = 0.014.$$

The number of nuclear transformations that occur in trabecular and cortical bone following intravenous administration of ^{89}Sr can be calculated from data given in Table 34 of the report of Marshall et al (1973):

$$U_{TB} = 86\,400 \times 5.57 \ \mathrm{Bq}^{-1}$$
$$U_{CB} = 86\,400 \times 6.88 \ \mathrm{Bq}^{-1}$$

where the factor of 86 400 is the number of seconds in 1 day, and corrects for the time units of days used in Table 34 of Marshall et al.

Combining the above numerical data in Equation (A1) gives for the irradiation of red marrow by ^{89}Sr in trabecular bone:

$$D_{RM}(TB) = 1.26 \times 10^{-8} \ \mathrm{Gy\,Bq}^{-1}$$
$$= 1.26 \ \mathrm{cGy\,MBq}^{-1}$$

and for the irradiation of red marrow by ^{89}Sr in cortical bone:

$$D_{RM}(CB) = 0.05 \times 10^{-8} \ \mathrm{Gy\,Bq}^{-1}$$
$$= 0.05 \ \mathrm{cGy\,MBq}^{-1}.$$

The net absorbed dose to red marrow following intravenous administration of ^{89}Sr is therefore:

$$D_{RM} = 1.31 \ \mathrm{cGy\,MBq}^{-1} \qquad \text{(A2)}$$

Book reviews

NCI Monographs. Proceedings of the NIH Consensus Development Conference on Adjuvant Chemotherapy and Endocrine Therapy for Breast Cancer, Sept. 9–11, 1985. Ed. by M. E. Lippman, pp. 165, 1986 (National Institutes of Health, Bethesda), $8.50 (USA) $10.65 (other).
Stock No. 017–042–00190–1

This monograph is taken from the proceedings of a National Institutes of Health consensus development conference on adjuvant chemotherapy and endocrine therapy for breast cancer. Nearly all those involved in adjuvant trials attended the meeting, which was held in Washington in September 1985. There are papers on the assessment of clinical trials, steroid hormone receptors, cell kinetics and pathology, as well as the results of some of the major trials. A paper was also read by Richard Peto (Oxford) on his group's conclusions from combining the results of all controlled adjuvant trials in breast cancer, but is not included in the monograph. A consensus panel of lay and expert opinion listened to all the talks (of which Peto's was the most important) and at the end of the meeting produced a statement which is regarded as the optimum guidelines for the adjuvant treatment of breast cancer. The conclusion of the panel was that all patients and their physicians should be strongly encouraged to participate in controlled clinical trials. Outside the context of clinical trials the panel concluded, from the summary of the results of trials, that patients without involvement of axillary nodes should not receive adjuvant therapy: post-menopausal patients with involved nodes should receive adjuvant tamoxifen and pre-menopausal patients with involved nodes adjuvant chemotherapy.

This is a reasonable reflection of current thinking, but it still remains to be established whether chemotherapy is more beneficial than endocrine therapy in pre-menopausal women: both types of treatment were reported to reduce the chances of death by between 20% and 30% in Peto's overview.

New drugs and new approaches are required if treatment is to become more effective. The monograph is a tribute to the high quality of clinical investigation in this field and provides a useful overview for those wishing to learn about the latest results of some of the important studies.

A. Howell

Screening for Cancer. Ed. by A. B. Miller, pp. xx+458, 1985 (Academic Press, London), £65.00.
ISBN 0–12–496720–5

For a condition where there is no effective means of prevention and no effective cure of established disease, screening to diagnose and arrest the disease early in its natural history offers the only hope. Regrettably, most cancers still fall into the "no prevention, no cure" category and there is, therefore, considerable interest in population screening for cancers of various sites. This book provides a comprehensive account of the state of the art in relation to various cancer screening programmes in the developed world.

Just because a cancer test is suitable for application to the public, does not necessarily mean that a screening programme using it is going to be successful. The programme needs to be evaluated just as rigorously as does a new form of treatment, and preferably by a controlled trial in which subjects are randomly allocated to a screening or a no-screening arm. The principles of evaluation are thoroughly explained in a series of chapters which include the complexities of selective screening of high-risk groups, and the science of cost–benefit analysis. There follows a series of chapters on the technical aspects of different tests, including radiography and other imaging techniques for cancers of the lung, breast and stomach. The final section of the book reviews the effectiveness of screening programmes for different sites. Despite the obvious enthusiasm of the various contributors, it is disappointing to find that no cancer screening programme has been unequivocally successful and that for many the necessary evaluation is incomplete.

This book will prove useful for community physicians and others in public health planning, for whom it can serve both as a textbook on the methodology of screening evaluation, and as a practical guide to what is, or is not, worth implementing. Specialists in various branches of diagnostic medicine will also find it a useful reference source on the ways in which tests can be adapted for mass application without loss of quality. Those involved in cancer treatment will find it an instructive, if somewhat disappointing, account of a theoretical way of controlling cancer mortality.

J. Chamberlain

1987, *The British Journal of Radiology*, 60, 261–268 MARCH 1987

Local control of Ewing's sarcoma: an analysis of 67 patients

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ABSTRACT

Local control of Ewing's sarcoma was analysed in a series of 67 patients treated by surgery and/or radiotherapy as well as combination chemotherapy. Radiotherapy was employed with or without surgery in 60 patients and produced an overall local control rate of 55%; complete excision of the primary lesion seemed to be beneficial. There was a marked variation in control rates depending on the site of the primary lesion. limb 85%, rib 53%, pelvis 31% and other sites 33%. Primary tumours greater than 10 cm in diameter were significantly less likely to be controlled. Using daily fractions of approximately 180 cGy, total doses in excess of 6000 cGy seem more likely to produce serious late morbidity and may not increase the local control rate. No cases of second malignancy arising in irradiated tissue have been observed to date, but one patient developed acute lymphoblastic leukaemia.

In his description of "diffuse endothelioma of bone" James Ewing (1921) noted amongst its other characteristics that the tumour is "highly susceptible to radium". For the next 50 years, radiotherapy continued to be the predominant form of treatment for Ewing's sarcoma, but about 80% of the patients so managed died from metastatic disease within 2 years (Chabora et al, 1976).

The outlook for patients with Ewing's sarcoma has improved dramatically in the last 15 years with the advent of intensive multidrug, multicycle chemotherapy. Adjuvant chemotherapy of this type when combined with radical radiotherapy to the primary tumour has resulted in the probable cure of 60–70% of patients with a distal limb primary (Kinsella et al, 1984). There is a suggestion too that the local control rates have improved over those achieved with radiotherapy alone (Chabora et al, 1976; Perez et al, 1981).

In the past few years, the traditional place of radiation as the best means to eradicate the primary tumours has come under scrutiny (Kinsella et al, 1984; Thomas et al, 1984). Several papers (Lewis et al, 1984; Rosen, 1978; Marcove et al, 1980; Li et al, 1983) from the Memorial Sloan-Kettering Cancer Center have advocated a greater role for surgery, either because the local recurrence rate with radiotherapy alone was disappointingly high, or because local control with irradiation was achieved only at the cost of severe functional impairment.

The greater numbers of long-term survivors from Ewing's sarcoma increase the likelihood that second malignancies due to treatment will occur and this risk must be assessed.

In order to provide further data on the efficacy of radiotherapy as a means of gaining permanent local control and on its disadvantages in terms of serious late morbidity, the records of patients treated for Ewing's sarcoma at St Bartholomew's Hospital (SBH) and at the Hospital for Sick Children, Great Ormond Street (GOS), were reviewed.

PATIENTS AND METHODS

A total of 76 patients with histologically proven Ewing's sarcoma were treated with multidrug chemotherapy at SBH or GOS between 1973 and 1984. The main drugs used in combination were cyclophosphamide, vincristine, dactinomycin and doxorubicin; some patients received additional treatment with high-dose melphalan or etoposide. Nine patients were excluded either because they presented with widespread metastatic disease and received no definitive local therapy (four patients) or because they relapsed after initial treatment elsewhere (four patients) or because the case notes were lost (one patient). Sixty-seven patients remained for analysis who had received radical treatment to their primary tumour either by radiotherapy (36 patients), surgery (seven patients) or both (24 patients).

The integration of the various forms of treatment varied. For pelvic and rib primaries all but one patient received combination chemotherapy first, in an attempt to reduce the bulk of the primary tumour and thereby facilitate subsequent local treatment. In seven patients with distal limb primaries it was elected to carry out amputation or resection as an initial step; 18 out of 20 patients with limb tumours treated by radical radiotherapy received prior chemotherapy.

Thirty-six of the 67 patients were male and 31 were female and their ages at the time of diagnosis ranged from 4 months to 33 years (median 11 years). The distribution of primary tumours is shown in Fig. 1 and it should be noted that nine patients had evidence of distant metastases (lung, lymph node, bone marrow and

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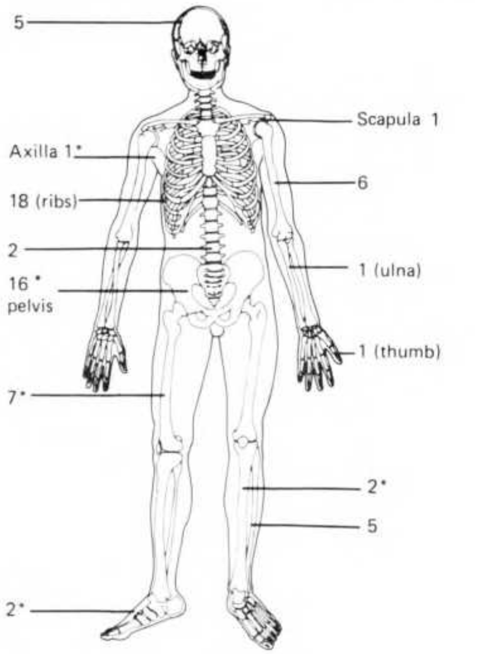

*Total includes one extra-skeletal Ewing's sarcoma

FIG. 1.

Distribution of Ewing's sarcoma.

bone) at diagnosis. These nine patients still received radical radiotherapy to the primary tumour and have therefore been included in the study. This series is unusual in having a preponderance of rib (27%) and low frequency of femoral (9%) lesions. Of 18 rib primaries only four were localised tumours with a small soft-tissue component; the other 14 had regional disease with extension into the pleural cavity. There were five cases of extra-osseous Ewing's sarcoma.

Surgery

Limbs. Nine patients underwent operations that comprised wide local excision of extra-osseous Ewing's sarcoma (three cases), through knee amputation (two cases), fibulectomy (two cases, one sparing the lateral malleolus), one thumb amputation and one foot amputation.

Ribs. At some stage, 16 out of 18 patients underwent resection of their primary rib tumour and associated soft-tissue mass.

Pelvis. Surgical resection was attempted in only one patient out of 16. In two patients absorbable mesh was used (Plowman et al, 1984) to displace loops of small bowel from the pelvis during high-dose post-operative radiotherapy.

Other sites. Five patients with Ewing's sarcoma at various sites (orbit two, vertebra two and sinuses one) underwent surgical resection of their primary tumour.

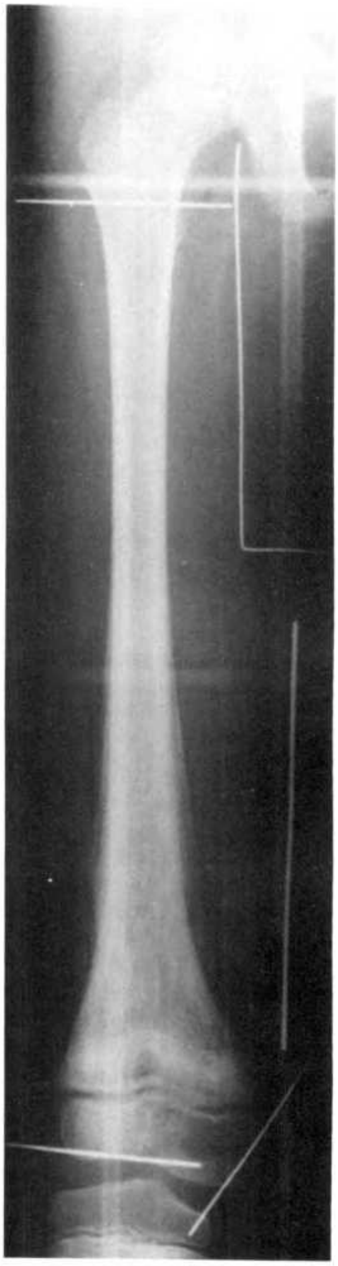

FIG. 2.

Simulation film demonstrating a Phase 1 radiotherapy field sparing the proximal epiphyses.

Radiotherapy

All patients receiving radiotherapy were treated on megavoltage equipment at SBH, having undergone careful simulation and planning.

Limbs. The four patients who underwent an amputation received no radiotherapy; the other 20 patients did. In 19, parallel opposed portals (POP) were used. The conventional technique of irradiating the whole bone to 30–40 Gy followed by a boost dose of 15–20 Gy to the primary site was used in all but five cases. Following the evidence of the Intergroup

Ewing's Sarcoma Study (IESS) (Perez et al, 1981), the uninvolved epiphysis of a long bone has been excluded in two recent cases (Fig. 2) to reduce the stunting of growth due to radiation. Except in one case, a corridor of the limb has been left unirradiated to prevent constriction by a circumferential band of fibrosis Great care is taken to ensure the reproducibility of the treatment set-up and light-weight casts are now used to maintain the limb in a constant position. The median tumour dose was 52 5 (range 43–65) Gy given in daily fractions of 184 cGy (median)

Ribs. Thirteen out of 18 patients received local treatment with both surgery and radiotherapy; in four patients the radiotherapy was completed pre-operatively, in four cases rib resection was sandwiched between a split course of radiotherapy, and the remaining five patients received radiotherapy post-operatively only. Of the remaining patients, two were treated by radiotherapy alone and three by surgery.

The arrangement of radiation portals and the volume of tissue treated were more varied than in the limb tumours, largely as a result of difficulties in irradiating a whole rib without producing unacceptable damage to the underlying lung and heart. Anterior and posterior POPs were again the most common choice (11 patients), but tangential fields with compensators and single fields using high-energy electrons were also employed The four patients irradiated pre-operatively received a median tumour dose of 30 Gy, whereas the other irradiated patients received a median dose of 46 (range 40–65)Gy; the median daily fraction was 175 cGy

Pelvis All 16 patients with pelvic tumours underwent radiotherapy; in 12 cases anterior and posterior POPs were employed. The initial treatment volume was based on the apparent tumour size before any chemotherapy. In six cases the volume of irradiated tissue was reduced after an initial dose of 25–45 Gy. A CT scan was available to assist with planning in 11 patients. The median tumour dose was 54 (range 40–60) Gy; the median daily fraction was 170 cGy.

Other sites. All nine patients received radical radiotherapy, five in conjunction with surgical resection. In planning the radiotherapy, the same basic tenets were followed· the primary tumour plus any soft-tissue extension plus several centimetres of apparently normal tissue were to be treated to a uniform dose. The median dose was 53 (range 35–60) Gy; the median daily fraction was 186 cGy; treatment volumes were reduced in four patients after 35–50 Gy.

The records of each patient were assessed for size of the primary tumour and its soft-tissue extent, the response to treatment, immediate and delayed morbidity from treatment, the duration of remission and the site(s) of relapse. The status of the patients on May 1, 1985, was established; eight patients were lost to follow-up after a median of 17 months. An autopsy was performed on only one patient.

RESULTS

Details of the primary site, the size (maximum dimension), the soft-tissue extent of the tumour and the

TABLE I

SITE AND EXTENT OF EWING'S SARCOMA AT DIAGNOSIS

Site of primary (No)	Size of primary		Soft-tissue extent		Metastases at diagnosis
	< 10 cm	> 10 cm	Small or none (< 2 cm)	Large (> 2 cm)	
Limbs					
Femur* (7†)	1	5	2	4	Lymph node (1)
Humerus (6)	4	2	3	3	Lung (1)
Fibula (5)	3	2	3	2	
Tibia (2†)	1	1		2	
Foot (2†)	2	0	1	1	
Ulna (1)	1	0	1	0	
Thumb (1)	1	0	1	0	
Totals (24)	13	10	11	12	2
Ribs (18)	5	13	4	14	Lung (1)
Pelvis					
Ilium (6†)	1	5	0	6	
Sacrum (5)	3	2	1	4	Lung (1)
Pubis (3)	0	3	0	3	Lung & lymph node (1)
Ischium (2)	0	2	0	2	Bone (1), lymph node & marrow (1)
Totals (16)	4	12	1	15	4
Other sites					
Shoulder (2†)	1	1	0	2	
Orbit (2)	2	0	0	2	
Vertebrae (2)	0	2	0	2	Marrow (1)
Skull (3)	3	0	0	3	Lymph node (1)
Totals (9)	6	3	0	9	2

*Dimensions of one tumour unrecorded

†Total includes one extraosseous Ewing's sarcoma.

presence of metastatic disease at diagnosis, are given in Table I. At diagnosis, limb tumours (54%) were more likely than rib (27%) or pelvic (25%) primaries to be less than 10 cm in diameter. The disparity in soft-tissue extent was even more marked, with 100% of pelvic tumours and 78% of rib tumours showing appreciable soft-tissue involvement whereas 50% of limb primaries did so. Ewing's sarcoma at other sites tended to be smaller (67% less than 10 cm) but all showed regional soft-tissue disease. The percentage of metastatic disease at diagnosis was: limb 8%, rib 7%, pelvis 27% and other sites 22%.

Response to treatment

Surgery. Surgical resection of nine limb tumours was considered to be complete histologically in all cases. Complete excision of a rib primary was obtained in nine out of 16 patients and this did not just depend on the extent of regional disease (two of four tumours without appreciable soft-tissue involvement were not completely excised). Three patients with rib primaries were managed with surgery alone and two subsequently had local recurrences. Resection of pelvic tumour was attempted in only one patient and was incomplete; similarly, surgery in five patients with Ewing's sarcoma at other sites achieved debulking rather than complete removal.

Radiotherapy. The response of Ewing's sarcoma to radiotherapy is difficult to assess clinically and radiologically (Taber et al, 1983). All the primaries in bone initially showed bone destruction and periosteal reaction on plain radiographs. Following radiotherapy, serial radiographs in responsive cases tended to show a marked decrease in periosteal reaction after 1–9 months and bone reconstitution with sclerosis after 5–12 months. Patients whose radiographs conformed to this pattern and were free of disease by all other criteria were classed as complete responders.

Table II shows the rate of local relapse by site and the median time to relapse following the completion of radiotherapy, and the same data are displayed in Fig. 3. The overall local relapse rate was 45% and this included seven patients (12%) in whom the primary tumour was never controlled. Fifteen patients (25%) experienced a local relapse in isolation; another 12 patients who relapsed locally also developed distant metastases at some time. The local relapse rates, by site, following radiotherapy were limb 15%, rib 47%, pelvis 69% and other sites 67%. Only one patient (5%) had an isolated limb recurrence compared with rib 27%, pelvis 37% and other sites 44%.

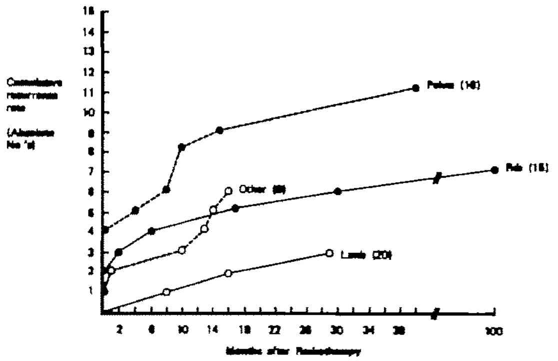

FIG. 3.

Cumulative local recurrences following radiotherapy with or without surgery by site of origin.

The three limb recurrences (fibula, femur, humerus) were all at the original site of disease in bone which had been irradiated to at least 55 Gy. No local relapses were seen in five patients given radiotherapy as an adjuvant treatment following complete excision of the limb tumour.

Of the three patients with localised rib Ewing's sarcoma who received radiotherapy, two remained in complete remission after an average period of 58 months. Twelve patients with regional pleural disease underwent surgery and radiotherapy but two were never controlled locally. Four had a subsequent local recurrence after a median time of 18 months and six remained controlled locally for 4–97 months (median 50). Of the eight patients who remained under local control following radiotherapy, five underwent surgical resection that was histologically complete at some stage. By contrast, only two out of seven patients who failed locally had had a complete resection of tumour.

Figure 3 shows that local failure in the pelvis tended

TABLE II

LOCAL RELAPSE IN PATIENTS RECEIVING RADIOTHERAPY

Site of Ewing's sarcoma	Total No receiving RT	No with local relapse and (No with local relapse only)	Median time from RT to local relapse (months)	Median tumour dose in local relapse cases
Limbs	20	3 (1)	27	60 Gy (55–65)
Ribs	15	7 (4)	6	45 Gy (25–55)
Pelvis	16	11 (6)	6	50 Gy (40–55)
Others	9	6 (4)	12	52 Gy (35–60)

TABLE III

Radiation dose and tumour response

Site		25–39 Gy	40–49 Gy	50–59 Gy	60–65 Gy
Limbs	No of patients	0	2	13	5
	No. of local recurrences	0	0	1	2
Ribs	No. of patients	3	8	3	1
	No. of local recurrences	1	4	2	0
Pelvis	No. of patients	0	2	13	1
	No. of local recurrences	0	2	9	0
Other	No of patients	1	2	5	1
	No. of local recurrences	1	1	3	1
All sites	No. of patients	4	14	34	8
	No. of local recurrences	2	7	15	3

to occur soon after the completion of radical radiotherapy and that four patients never achieved a complete response. Only one of the five patients at present apparently controlled by radiotherapy has been followed up for more than 2 years.

Table III shows that there is no evidence of a dose–response relationship at any site, but the numbers in individual categories are small.

The rates for local control following radiotherapy are shown in Table IV according to the size and soft-tissue extent of the primary tumour. The size of one tumour could not be accurately established from the records. Tumours 10 cm or more in diameter were significantly less likely to be controlled following radiotherapy ($\chi^2 = 5.51, p < 0.05$), whereas the influence of extension into surrounding soft tissue was not significant ($\chi^2 = 2.42$). Only one of the five extraskeletal Ewing's sarcoma recurred and, if these cases are excluded, neither the size nor soft-tissue extent has a statistically significant effect.

Morbidity from treatment

Surgery. Amputation in a child or adolescent must obviously cause psychological distress, but the four patients who underwent such an operation seemed to adjust to the situation remarkably quickly. One girl who had a through knee amputation had to wait 7 months for a satisfactory prosthesis and developed lung metastases 1 month later. The only significant morbidity from a lesser operation was a girl whose lateral popliteal nerve was sacrificed during a fibulectomy and who later underwent successful reconstructive surgery for an equino-varus deformity.

TABLE IV

Local control following radiotherapy by tumour size and soft-tissue extent

	Size of primary		Soft-tissue extent	
	< 10 cm	> 10 cm	< 2 cm	> 2 cm
Local recurrence	7	20	3	24
No recurrence	18	14	9	24

Scoliosis in one patient seemed to be due predominantly to surgery. He had undergone, in succession, a dorsal laminectomy, resection of ribs 1–4 and a thoracotomy.

Radiotherapy: early morbidity. This was mainly confined to skin reactions, amounting to moist desquamation in 12 patients (seven of whom had limb primaries). One patient developed a troublesome proctitis and another with a primary in the frontal sinus and orbit developed a detached retina shortly after radiotherapy was completed.

Radiotherapy: late morbidity. The details of the orthopaedic problems that were apparent 4 months to 5 years after the completion of radiotherapy in patients with limb tumours are given in Table V; the tumour dose is also given for each case. The resulting functional impairment was graded as follows:

Grade 1. Minor functional limitation or normal function but with cosmetic/radiological abnormality.

Grade 2. Moderate functional disability (shortening < 4 cm, moderate pain, contractures).

Grade 3. Severe disability (shortening > 4 cm, pathological fracture, chronic pain, severe atrophy).

It will be noted that the three patients who later sustained pathological fractures all received 60 Gy or more.

Three patients with rib tumours, apart from the boy mentioned above, developed scoliosis, but this did not become apparent until 2 years after radiotherapy. In two cases the tumour doses were high: one patient received 65 Gy initially, the other had the primary site re-irradiated for a large local recurrence and received a total dose of 100 Gy. The latter patient is in complete remission 5 years after re-treatment but has asymptomatic pulmonary fibrosis. The two "high-dose" patients were young girls and the irradiated breast failed to develop.

The only serious late damage seen from radiotherapy in patients with pelvic tumours was a girl who

TABLE V

Late morbidity in limbs due to radiotherapy

Patient	Age at RT (years)	Site of Ewing's sarcoma	Radiation dose	Late morbidity	Grade of severity
3	12	Fibula	55 Gy	Some loss of movement at ankle	1
8	13	Fibula	50 Gy	Tibial necrosis (radiologically); runs normally	1
10	12	Femur	55 Gy	4 cm shortening and wasted thigh	2
12	11	Humerus	60 Gy	20° elbow fixed flexion, shortening	1
13	12	Humerus	65 Gy	Pathological fracture, wasting	3
16	13	Fibula	50 Gy	2 cm shortening, genu valgum	2
17	13	Femur	60 Gy	Wasting of thigh	1
19	10	Humerus	65 Gy	Pathological fracture	3
20	7	Femur	60 Gy	3 cm shortening, pathological fracture	3

developed severe haematuria due to radiation cystitis. She received a dose of 55 Gy, and cyclophosphamide had been administered during the early part of her course.

No significant late side-effects have been observed in four patients with tumours at other sites followed up for 2–5 years after radiotherapy.

Second malignancy

One patient treated for a rib primary developed acute lymphoblastic leukaemia (ALL) 5 years after Ewing's sarcoma was diagnosed. During that time he had initial radiotherapy (45 Gy) and chemotherapy (vincristine, dactinomycin and cyclophosphamide for 16 courses), and then etoposide (multiple courses) and re-irradiation (45 Gy) for a relapse outside the original radiotherapy field. Following further chemotherapy the ALL completely remitted for 3½ years until he died from metastatic Ewing's sarcoma.

No case of a second malignant tumour developing within an irradiated field has been observed.

Discussion

Although Ewing's sarcoma is a systemic disease and the greatest advance in terms of its treatment has been the development of effective adjuvant chemotherapy that can eradicate micrometastases in a substantial proportion of patients, the need to control the primary tumour by local means remains. The present series represents a group of patients who have all received medical treatment with what are generally considered to be the best drugs available and most received several cycles of chemotherapy before local therapy. The initial shrinkage of the primary tumour due to chemotherapy in general facilitates subsequent ablation. However, it may also create difficulties, notably the temptation to omit either radiotherapy or surgery after an already reduced tumour mass seems to have been completely controlled. In this series we have seen the recurrence of a fibula primary after it had been decided not to resect the bone and of a localised rib tumour after post-operative radiotherapy had been witheld. We note that the most recent report (Ong et al, 1984) from the Memorial Sloan-Kettering Cancer Center concluded that "postoperative radiation does significantly decrease the rate of local recurrence" and advocates that all three modalities should be used in treatment where possible.

Limbs

The local control rate of 85% after a median surveillance of 30 months for limb tumours treated by radiotherapy concurs with other modern series (Perez et al, 1981; Kinsella et al, 1984). There have been no local recurrences when radiotherapy has been given following surgical removal of the limb tumour. The three failures seen following radiotherapy were all in portions of bone involved by Ewing's sarcoma initially, in keeping with the observation of Suit (1975). Although some earlier reviews (Suit, 1975; Chabora et al, 1976) suggested that better control resulted from radiation doses above 60 Gy, our data do not support this contention and, in common with the IESS (Perez et al, 1981), we found no clear dose–response relationship. It should be noted, however, that for some categories of dose the numbers of patients were small (Table III).

Late morbidity did seem to be dose-related (Table V) but has not been severe enough to warrant amputation in any instance. We would agree with others (Thomas et al, 1984) that radiotherapy for femoral lesions in particular can give rise to functional problems later: two out of four patients followed for more than 2 years after treatment have had moderate or severe deficits, but still less than the morbidity from primary amputation. The inclusion of the whole femur in the first phase of radiation treatment will lead to variable shortening depending on the patient's age, but if, as now seems possible, the epiphysis away from an eccentric primary can be safely excluded, the later discrepancy in growth should be reduced. Table VI summarises the shortening that may be expected from irradiation of long bones at different ages depending on

TABLE VI

LENGTH AND PREDICTED GROWTH OF FEMUR AND TIBIA

	Age (years)	Boys				Girls			
		Mean length (cm)	Expected total growth (cm)	Growth from proximal epiphysis (cm)	Growth from distal epiphysis (cm)	Mean length (cm)	Expected total growth (cm)	Growth from proximal epiphysis (cm)	Growth from distal epiphysis (cm)
Femur	6	28	19	6	13	28	15	4.5	10.5
	8	32	15	4.5	10.5	33	11	4	7
	10	36	11	3.5	7.5	37	7	2.5	4.5
	12	40	7	2	5	41	3	1	2
	14	44	3	1	2	43	0.5	0.5	0
	16	46	0.5	0	0.5	44	0	0	0
Tibia	6	22	15	9	6	23	12	7	5
	8	25	12	7	5	26	9	5	4
	10	29	9	5	4	29	6	3.5	2.5
	12	32	5	3	2	33	2	1	1
	14	35	2	1.5	0.5	34	0.5	0.5	0
	16	37	0	0	0	35	0	0	0

whether an epiphysis can be spared or not (Anderson et al, 1963).

The opportunity to spare one epiphysis during radiotherapy to a long bone can dramatically reduce the ultimate shortening. For example, a 6-year-old boy with a tumour in the upper femur would expect to have 19 cm of shortening at maturity if growth at both epiphyses ceased (Table VI). However, if the distal epiphysis can be excluded from the radiotherapy field, the shortening is likely to be about 6 cm. The modern method of chondrodiatasis or epiphyseal distraction (Monticelli et al, 1981) offers the possibility of lengthening the bone in its unirradiated part and overcoming deficits of a few centimetres. Patients for such a procedure would have to be very carefully selected.

Unlike an earlier report (Lewis et al, 1977), irradiation of lesions below the knee has not produced major orthopaedic problems, but we would agree that excellent functional results in these sites (Jentzsch et al, 1981) depend on meticulous planning and treatment with the avoidance of large dose fractions or excessive total doses of radiation.

In general we believe that the patients with Ewing's sarcoma benefit from limb conservation. Radiotherapy using shrinking fields (Perez et al, 1981; Thomas et al, 1984) to deliver a dose of 5000–5500 cGy to the primary tumour in 180–200 cGy fractions produces a high local control rate without unacceptable morbidity.

Ribs

Ewing's sarcoma rarely arises in rib and the present collection of 18 patients represents the second largest group in the world literature. Compared with the larger IESS series (Thomas et al, 1983), the proportion of cases with localised rib disease (four patients) was low. In several cases the extraskeletal mass component was so large that the entire hemithorax had to be included in the Phase I radiotherapy volume. In the IESS report, local recurrence was observed in only one of 21 patients with localised disease. In the present series, two patients with localised disease had a recurrence (one having received no radiotherapy), and half the patients with regional disease again remained controlled. Like the IESS study, our data suggest that complete surgical excision in addition to radiotherapy enhances the prospect of local control, but the confounding effect of tumour size cannot be excluded.

The radiation doses employed for patients with rib Ewing's sarcoma were varied in this series, but no dose–response relationship was observed. Two patients with large primaries who received three cycles of combination chemotherapy and 30 Gy radiation had no histological evidence of viable tumour at subsequent surgery. However, as with limb primaries, the late morbidity from radiotherapy did seem to be due to high doses in some cases. No examples of clinically significant cardiomyopathy or pulmonary fibrosis have been observed to date.

Pelvis

The poor prognosis for patients with pelvic Ewing's sarcoma is well documented in the literature (*e.g.* Chabora et al, 1976; Rosen, 1978) and many think that the large size of these tumours at diagnosis is a major reason (Marcus et al, 1984; Evans et al, 1985). Our results confirm the significance of tumour size but not of soft-tissue extent (Mendenhall et al, 1983). Three-quarters of the pelvic primaries in this series were more than 10 cm in diameter and the overall local control rate of 31% was correspondingly poor. Indeed, the true picture may be even more dismal since it seems likely that, had autopsies been carried out on patients dying from disseminated disease, small local recurrences undetected during life would have been found (Telles et al, 1984). It may be that the lack of a dose–response relationship for pelvic primaries just reflects that the range of doses that we were able to give was insufficient to sterilise very bulky tumours. The local control rate might have been higher had a more aggressive surgical policy been adopted: *en bloc* resection of pelvic tumour in addition to chemotherapy and radiotherapy has been reported (Li et al, 1983) to reduce the rate of local recurrence, although others (Bacci et al, 1982) found that it made no difference. The most recent IESS report (Evans et al, 1985) found a trend towards better control after complete excision, but this did not reach statistical significance. In future we intend to follow a more aggressive surgical policy towards pelvic tumours and to gain further experience with the technique of bowel displacement prior to radical radiotherapy.

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Improved total-body irradiation dosimetry

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ABSTRACT

The total-body irradiation (TBI) technique at St Bartholomew's Hospital has been developed to improve dose homogeneity within the patient. Using a standard 6 MV linear accelerator in an orthodox-sized treatment room, the midpoint doses in head, neck, shoulders, mid-mediastinum, pelvis, knees and ankles are ±5% of that of the umbilicus in our current technique. This homogeneity has been achieved by a four-field technique, a reproducible patient set-up, careful use of a new bolus material and an additional beam-flattening filter mounted near the machine head. In addition, thermoluminescent dosimetric data collected at a test irradiation before TBI are used to influence field weightings and further improve dosimetry. This individualised and empirical TBI technique has dosimetric advantages over theoretical TBI dosimetric considerations in reducing dose gradients within the patient. These advantages are discussed.

Total-body irradiation (TBI) has become the established and preferred means of effecting bone marrow ablation before bone marrow transplantation (BMT) and this form of therapy is currently widely practised for poor-risk acute leukaemia. Total-body irradiation is not only more toxic to the bone marrow than many drugs, but it penetrates all body tissues (*i.e.* there are no sanctuary sites), and being a mode of therapy distinct from cytotoxic drugs, it is quite probable that some chemoresistant leukaemic cells will remain radiosensitive. Substantial evidence is accumulating to suggest that TBI in conjunction with BMT represents the best available treatment for acute myelogenous leukaemia in first remission and acute lymphoblastic leukaemia patients in second or subsequent remissions (O'Reilly, 1983).

Many radiotherapeutic publications on TBI have concentrated on the dose prescription (including dose-rate considerations) and these aspects of TBI have often eclipsed the other major radiotherapeutic ingredient, the dosimetry (Kim et al, 1980; Barrett, 1982). From the literature, it is clear that there are wide variations in the dose received by the different parts of the body in the TBI techniques of various centres. Thus, the maximum dose may exceed the minimum dose by more than 20–30% in many cases, and attempts at tissue compensation may still allow inhomogeneities of the order of 15% along the length of the body (Kim et al, 1980; Galvin, 1983; Shank, 1983; Van Dyk, 1983). Large field sizes do not circumvent all the problems, and aspects such as beam profile, off-axis data and skin-sparing are frequently ignored.

At St Bartholomew's Hospital, it is believed that dose homogeneity during TBI is important with regard to both leukaemic cell kill and normal tissue morbidity and that the dose distribution should be understood fully, so that inhomogeneities may be minimised.

Although others have obtained dosimetric data for TBI from the conventional basic physics data for the machine used (Galvin, 1983; Van Dyk, 1983), there are problems with many of the presumptions implicit in such calculations. In TBI, the whole body is subtended by the radiation field and thus this radiotherapy technique differs from all others, *vide infra*.

In this paper we describe the method by which the TBI basic data-set has been obtained. Fundamental to our treatment approach is the dosimetric data collected for each patient at a test session. These data (basic/patient) are then used to plan the optimum therapy technique for the individual patient. We describe here the improving dosimetry as the technique has evolved.

METHOD AND PHYSICAL CONSIDERATIONS

The current technique, while being continually developed over the past 5 years, has always been based on the fundamental principle of an initial test irradiation preceding treatment. For dosimetric accuracy, reliance was placed on total reproducibility of set-up between test and treatment, together with confirmation that during treatment the machine output characteristics were consistent with those during the test. Thermoluminescent dosimetry (TLD) was used to establish both absolute dose and dose distribution within the patient.

Equipment

When the TBI programme was first implemented at this centre the limited field size available resulted in an overflexed semifetal position for the majority of patients. Further details of this "early technique" are reported elsewhere (Fitzgerald et al, 1982).

Following the installation of a new 6 MV accelerator (Varian, Clinac 6) in 1983, all subsequent TBI

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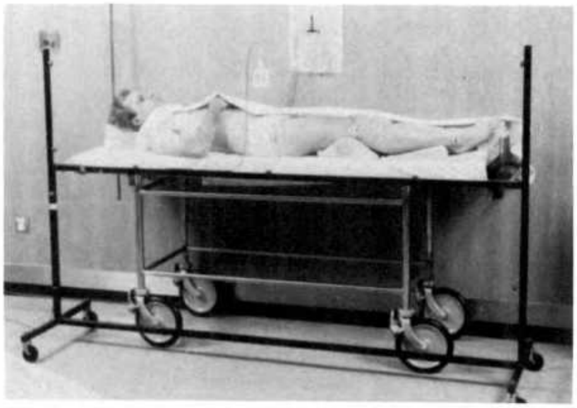

Fig. 1.
The current clinical set-up for TBI (supine position).

treatments have been carried out on this unit. A flat mobile couch (Fig. 1), specially equipped with stand-off spacers to maintain a consistent displacement from the room side-wall, was used to support the patient in these circumstances. For this subsequent procedure ("later technique") the approximate source-skin distance (SSD) was 380 cm, and at this distance the maximum effective field length was 180 cm across the field diagonal. The basic dosimetric data reported here refer to the "later technique".

Basic dosimetric data

The traditional techniques for recording basic data for external-beam therapy based on ionisation measurements in a large (usually 40 cm × 40 cm × 40 cm) water tank are inappropriate for TBI. In conventional beam dosimetry, provided the dosimetry tank size is larger than the field size, the former plays no part in the spatial distribution of dose and the variable parameter is field size. In TBI the beam completely subtends the patient and is of fixed size; variations occur because of changing patient dimensions.

Measurements made in preparation for a TBI programme must be performed under the same geometrical conditions as those necessary to treat the patients. By fixing the diaphragm setting and treatment distance, the number of interrelated parameters that need to be assessed is reduced. To some extent the actual parameters that need to be measured will depend upon the philosophy behind the dosimetry technique. The option of calculating target-volume doses throughout the whole of the body from pre-recorded basic data, taking into account patient shape, size and tissue heterogeneity, is a formidable task. Both Galvin (1983) and Van Dyk (1983) enumerate the difficulties associated with this technique, listing the many physical considerations that must be made in the computation. A simpler approach is to prescribe at a single point using central axis depth-dose data only; but in this case the dosimetric information is too limited. The technique we favour is based on measuring patient surface doses in order to compute midpoint doses in different sections. This requires rather fewer experimental data than in the first approach but provides more insight into the spatial distribution than the second, single-point technique.

The basic data that are necessary for the surface-dose measurement method which will enable correct prediction of midpoint doses are percentage depth doses including entrance and exit surface ionisation measurements. In addition, it is helpful to make measurements of beam profile in order to anticipate potential regions of high and low dose along the patient's length.

To provide realistic scatter conditions an approximately patient-sized phantom was used for all measurements. This was of a modular construction. The section contiguous to the measuring probe was composed of water-substitute plastic-resin slabs (Constantinou et al, 1982) varying in thickness from 0.5 mm up to 70 mm and enabling a total stack thickness of more than 400 mm. Slabs of the water-equivalent phantom (WEP) were available with moulded cavities to accept a 0.6 cm^3 thimble chamber and a 0.3 cm^3 thin-window chamber. Adjacent to this measurement probe section, plastic containers filled with water having external dimensions 24 cm × 24 cm × 40 cm were used side-on to simulate the scatter conditions. Judicious manipulation of these containers enabled the position of the measurement section within the phantom to be varied and the total phantom length to be increased to 150 cm.

Build-up and exit dose. Entrance- and exit-dose studies were carried out using a thin-window (2.3 mg cm^{-2}) coin-shaped ionisation chamber (Nuclear Enterprises NE type 2536/3) and the WEP, under TBI conditions. For entrance-dose studies the chamber was mounted conventionally with the thin window facing the radiation source and for exit-dose studies the window faced away. Use of this chamber arrangement at this centre was previously reported by Lambert et al (1983).

Build-up ionisation measurements at the entrance surface are shown in Fig. 2. With TBI treatment geometry, surface doses were found to be significantly higher than with normal treatment distances and field sizes. The effect on surface ionisation of the 1 cm-thick perspex screen interposed just in front of the treatment couch is also shown in Fig. 2 for a typical screen-to-phantom distance of 15 cm. No strong dependence on screen–phantom distance was found. For example, at a depth of 0.5 mm the ionisation relative to the maximum was found to be 0.995, 0.997 and 1.000 at screen-to-phantom distances of 25 cm, 15 cm and 10 cm, respectively. Off the beam central axis the relative surface ionisation was found to be slightly reduced, a ratio of 0.989 being measured 65 cm off axis at a depth of 0.5 mm relative to the dose maximum in this section.

Close to the exit surface the relative ionisation might be expected to fall as a result of the loss of electronic

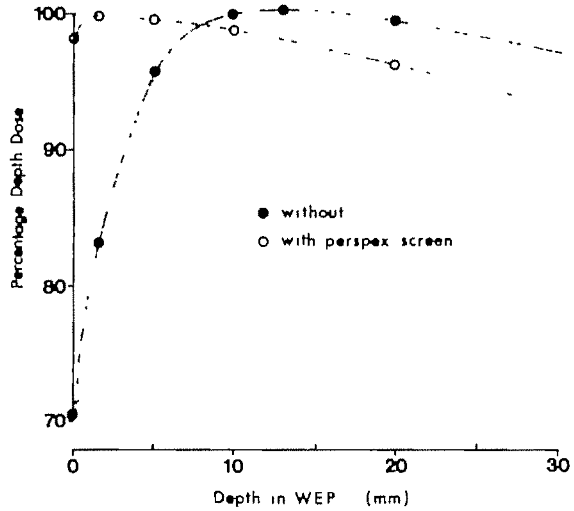

Fig. 2

Dose build-up curve at the TBI treatment distance without and with a 1 cm-thick perspex screen.

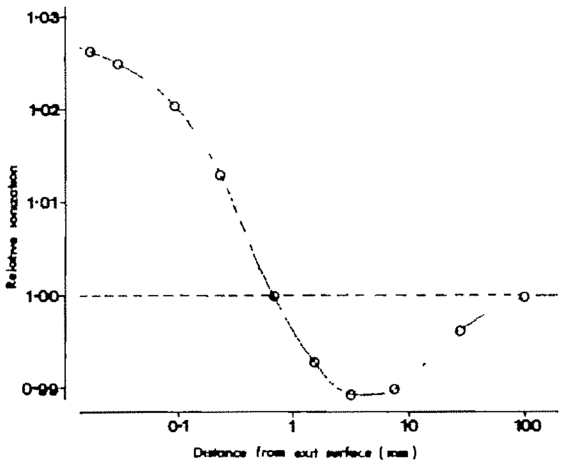

Fig. 3.

Variation of relative ionisation (normalised to the value obtained with full scatter) in the region of the exit surface Distance between phantom exit surface and wall was 20 cm.

equilibrium owing to the absence of backscattering material (Lambert et al, 1983). In practice this trend was found to be camouflaged by low-energy scatter from the adjacent treatment-room wall. The curve of relative ionisation (normalised to the value obtained with full unit-density scatter) versus distance from the exit surface is shown in Fig. 3. It should be noted that a dosemeter backed by 0.5 mm of unit-density material (see below) will overread relative to the same measurement made in an extended phantom by a factor of approximately 1.005.

Thus, surface dosemeters with 0.5 mm of unit-density build-up tend just to underestimate the maximum dose at the entrance surface and to record just higher than would be the dose at the same point in an extended phantom at the exit surface. The composite reading from surface dosemeters used with two opposed fields is likely to be extremely close to that predicted from basic depth-dose data by summing entrance and exit doses, taking the entrance dose to be 100% and the exit dose to be equal to the basic data value for the depth of the separation of the dosemeters. In our dosimetric calculations we make the assumption that the predicted and measured values are equal

Depth dose. Percentage depth doses (%DD) were measured using the NE type 2536 chamber. Measurements on the central axis were carried out for phantom lengths of 24 cm and 150 cm. With the measurement section displaced, %DD was also measured 65 cm lateral to the central axis of the beam in the longer phantom. The data are given in Table I. A small but demonstrable increase in %DD is observed with the longer phantom. As was expected, because of the obliquity of the primary radiation off axis and different scatter conditions, the two sets of figures for the longer phantom are slightly disparate, the off-axis values being lower at any depth.

The central axis percentage depth dose (CAX %DD) data were used in the following manner to enable prediction of midline patient doses. For different surface dosemeter (patient) separations a factor P_z was calculated.

$$P_z = 2\frac{D_{z/2}}{100+D_z}$$

where D_z = %DD at depth z cm and $D_{z/2}$ = %DD at depth $z/2$ (midpoint). Figure 4 illustrates the variation of P factor with patient separation z Making the assumption that entrance + exit dose was equal to $100+D_z$, the P factor was used to calculate midpoint doses from measured surface doses.

TABLE I

Central axis and off-axis percentage depth doses at the TBI treatment distance

Depth in phantom (cm)	Percentage depth dose		
	Central axis		65 cm off axis
	phantom length		
	24 cm	150 cm	
0.05	99 3	99.7	98.9
5.0	88 5	89.0	87.7
10 0	75.0	76.0	73 0
15.0	62.5	63.5	59.5
25.0	41 0	42.5	38.0
35.0	27.0	28.0	25.0

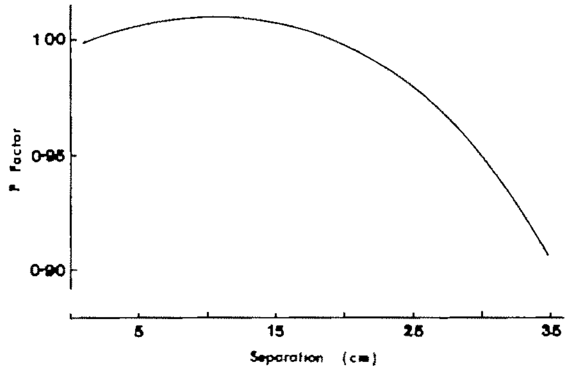

Fig. 4.

For parallel opposed fields the graph shows the ratio of midpoint to surface dose plotted against variation in sectional separation.

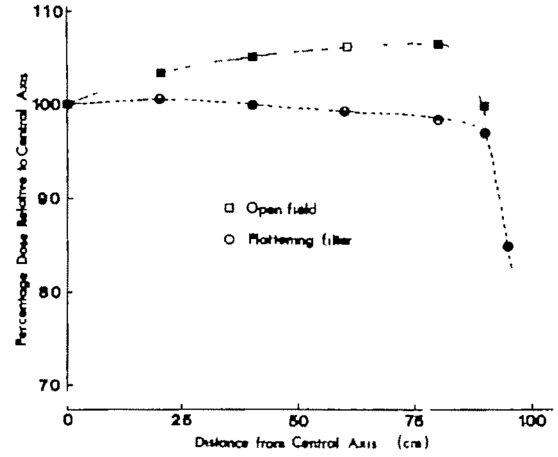

Fig. 5.

Diagonal half-beam profile measured at 10 cm depth for the open field and with the additional flattening filter

Beam profile. The inherent beam-flattening filter on a Varian 6/100 linear accelerator is designed to produce optimum beam uniformity for a 30 cm × 30 cm field (100 cm SSD at 10 cm depth). This can result in "overflatness" or "horns" at shallower depths and along the diagonals of larger fields at 10 cm depth. On our Varian machine, measurements made at 100 cm SSD, 10 cm deep with fully open diaphragms (40 cm × 40 cm) the maximum dose rate along the diagonals was found to be 4% higher than on the central axis. Similar results have been reported by Constantinou and Sternick (1984).

For TBI purposes, dose-profile measurements were carried out along the horizontal field diagonal at 10 cm depth in the representative body-sized WEP. The results of these measurements are shown in Fig. 5. Readings taken at symmetric points about the beam central axis have been averaged but were found to differ by not more than ±1.0%. The profile shows, as expected, that the overflatness reported above at 100 cm SSD was still apparent at TBI treatment distances but, in contrast to the suggestion of Goolden et al (1983), this was not found to be greatly increased.

As a consequence of this overflatness, those regions of the patient situated near the beam extremities (head, neck, feet and lower legs) might be expected to demonstrate a dose enhancement relative to the midfield sections. It should also be noted that, in general, these sections are cross-sectionally small relative to the umbilicus, further exacerbating the problem.

For these reasons it was decided to design an additional symmetric flattening filter to improve the beam uniformity characteristic for TBI use. This took the form of a set of ring-shaped, clear perspex laminates of varying radii bolted together as a single unit. The device was positively located in the accessory mount on the treatment head during irradiation. The resultant beam profile is shown in Fig. 5.

Thermoluminescent dosimetry procedure. Because the dosimetric precision of the treatment irradiation hinges ultimately on the accuracy obtained from the TLD technique, great care was taken with the procedure. The dosemeters used were extruded lithium fluoride (LiF) ribbon (Harshaw TLD 100) which were read out in an automatic reader (Vinten Toledo) interfaced to a microcomputer.

A low-temperature post-irradiation anneal (120°C for 16 s) was incorporated into the read-out cycle to minimise the effect of the patient's body temperature on the TLD material. For pre-irradiation annealing the LiF "chips" were placed on a lidded, anodised aluminium tray and heated using two separate ovens; initially for 1 h at 400°C and then for 2 h at 100°C. Particular care was taken in reproducing the final cooling conditions.

Two hundred chips were allocated solely for TBI use and each was labelled with a pencilled code number and annealed. An individual sensitivity calibration factor was determined by giving the chips a dose of 0.1 Gy, using a calibrated ionisation chamber for reference. Following this calibration dose and read-out, the chips were re-annealed. Those chips to be used for the TBI test (approximately 90 chips) were packaged in pairs in thin plastic sachets. Together with the tape that attaches the sachets to the patient, these 12 mm square plastic containers provide a build-up of 0.5 mm of approximately unit-density material for the chips.

Of the remainder of the original 200 chips, 20 were set aside for a second calibration: the so-called "batch" calibration. This determined how the mean sensitivity of these 20 chips taken as a whole had changed since the "full" calibration. Any change in the overall calibration of the batch was taken to reflect the change in sensitivity resulting from the second anneal. This batch calibration factor was then used to scale the individual calibration factors determined at the full calibration of the remainder of the chips.

Bolus material. For optimum dose homogeneity it is essential to provide a facility to compensate for large tissue deficits. Appositional bolus material was used.

The disadvantage of the traditional bolus material, Lincolnshire bolus (Lindsay & Stern, 1953), is that bags of the material are not sufficiently self-supporting and thus cannot retain a precise geometrical shape. Accordingly we have developed a malleable water-substitute material for megavoltage energies (subject of another publication in preparation). The material, a compound of soft paraffin and acrylic granules, is sealed in thin elastic polyurethane bags. At room temperature the consistency of these bags resembles that of soft Plasticine or putty and it can therefore be moulded around the patient and subsequently retain its shape.

Patient dosimetry

Treatment was planned to be given with the patient fully reclined in three distinct positions: supine for the lateral fields, right decubitus and left decubitus for the anterior/posterior (AP) fields. Comfort and positional reproduction were assisted by supporting the patient with foam blocks of various shapes and sizes, each with a unique identifying code. The details of the blocks used and their positions were recorded at testing and carefully reproduced at the time of treatment.

In the supine position the patient lies flat with arms across the chest as shown in Fig. 1. The bolus material was moulded around the neck and also between the spaced legs, where the total lateral separation of the upper thighs was maintained down to the ankles. In the lateral positions, head and back supports were used and the legs slightly flexed to aid stability. Once again, bolus was applied to the neck but not normally to the legs, apart from in the male patients where it was used around the scrotum to retain the scatter contribution. A record was made of the position of the light field centre relative to the umbilicus.

Test irradiation. Using the continuously variable pulse repetition frequency (PRF) control, the output rate was adjusted to an indicated rate of 130 monitor units (MU) min^{-1}. This corresponds to approximately 7.5 cGy min^{-1} at the mid-section of the patient. The total exposure time for the test was noted.

Latterly only two of the treatment positions have been test irradiated: supine and one lateral position. The midline dose distribution was determined from combined entrance and exit surface TLD measurements from the lateral fields and then from AP fields. Dosemeters were employed in eight transverse sections: head, neck, shoulder, mid-mediastinum, umbilicus, pelvis, knee and ankle. The dosemeters were positioned on the mid-coronal (lateral fields) or mid-sagittal (AP fields) line except in the thoracic sections where for the AP fields both right and left lungs were monitored. Sachets containing the LiF chips were taped directly to the patient's skin and covered with bolus only in the neck region.

While in the treatment positions, transverse separations of the patient were determined in all the dose-measurement planes. With the patient in the supine position, a machine setting of 40 MU was delivered to both lateral fields: the couch was rotated through 180° between fields, while the patient's attitude on the couch top was kept static. The procedure was repeated with 40 MU given to both anterior and posterior fields.

In addition to the integral dual dosimetry of the accelerator, two separate ionisation chamber systems were used to ensure constancy and linearity of output between the test and treatment sessions. One ionisation chamber was placed on the wall behind, but not shielded by, the patient and the second was attached to the distal side of the perspex screen (Fig. 1). Farmer dosemeters type NE 2570 were used in conjunction with the chambers.

Dose distribution. From the results of the test irradiation, absorbed doses were calculated in each of the measured sections. The longitudinal midpoint dose (MPD) distribution from the two tested positions were initially assessed separately. In the untested decubitus position the distribution was assumed to be identical to the tested side. This assumption was founded on previous experience gained by testing both sides.

For the parallel opposed fields the calculation was as follows: MPD in any section having a separation of x cm is given by

$$\mathrm{MPD} = \left(\frac{D_{01}+D_{02}}{2}\right)P_x$$

where D_{01} and D_{02} are opposite surface doses in that section measured by the LiF. P_x is the separation-dependent factor relating midpoint dose to surface dose. These correction factors were always incorporated into the MPD calculation irrespective of sectional dimension. In those sections where a volume of lung exists, a value of P based on the effective attenuation (related to the actual separation and the thickness of lung traversed) was used (see International Commission on Radiation Units and Measurements (ICRU), 1976). For example, the factor for a homogeneous section 30 cm thick is 0.95. However, if the section included 18 cm of traversed lung (estimated, or measured from CT scans), having an average relative density of 0.30, the assigned P factor, based on an effective separation of $(18\times0.3)+(30-18) = 17.4$ cm, would be 1.01.

Typical midline dose distributions for parallel opposed fields attained in both the supine and decubitus positions are shown in Fig. 6. These distributions are normalised to the MPD at the level of the umbilicus. The lines joining points are intended for clarification and are not indicative of the dose gradient between sections. It can be seen that, even with the benefit of the bolus, significant dose inhomogeneity still exists. The effect of combining these positions with different field

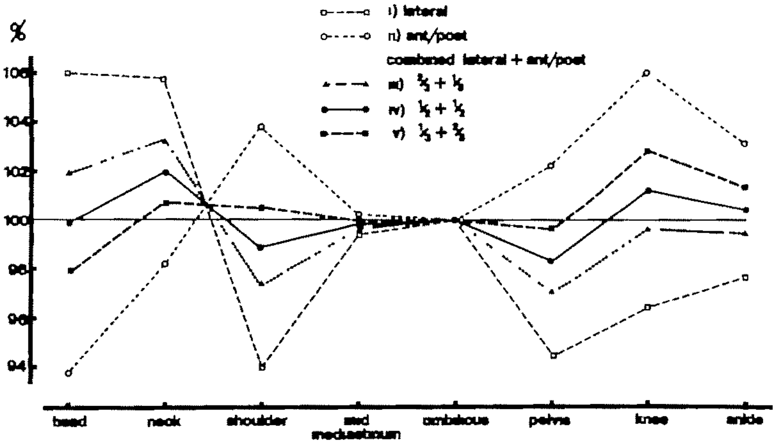

FIG 6

Midline dose distribution (normalised to the umbilicus) from parallel opposed (i) lateral and (ii) AP fields. The combination of fields of various weightings, (iii) 67% + 33%, (iv) 50% + 50% and (v) 33% + 67% being the respective contribution from the lateral and AP portals

weightings is also shown in Fig. 6. It is evident that, by sagacious application of weighting, an acceptable level of midline dose homogeneity can be achieved.

A computer program has been developed to optimise the field weightings to obtain the most uniform midline dose distribution. The algorithm sequentially summates the differences between the MPD in the measured sections and the MPD at the umbilicus, and determines what proportion of AP and lateral fields will minimise these differences. In addition, it is possible to apply weighted "significance factors" to all or any of the measured sections. These factors allow a component of subjective judgment to be interposed into a purely mathematical computation.

Treatment session. The treatment dose (D_p) was prescribed midpoint at the level of the umbilicus, the point of normalisation for the dose distribution. Machine unit setting necessary to give this dose (MU_p) was calculated directly from the relationship

$$MU_p = \frac{D_p}{D_T} \times MU_T$$

where D_T = the total umbilical MPD resulting from the test irradiation and MU_T = MU setting for the test. Correlation of machine output with MU setting over the range 40–999 MU (the maximum single exposure setting) was measured and found to be excellent (correlation coefficient = 0.999). In determining D_T, due consideration was given to the field weighting required to achieve the optimum midline distribution and the total MU_p setting was divided up accordingly.

Our "early" TBI technique included TLD measurements on the treatment day in addition to a test. The session was carried out in three phases. Measurements in all transverse sections were made during the first 10% of irradiation (all fields being treated to their respective weight). The LiF chips were processed and the results analysed over the next planned 80% phase, enabling any apparent necessary dose or MU setting adjustments to be made in the final 10% stage.

More recently, the therapy session has been undertaken in two phases. All positions/fields were irradiated to 50% of the planned monitor unit setting (MU_p). Readings from the additional ionisation chambers indicate the accuracy and linearity of machine output compared with the test session. Discrepancies between the actual and predicted output were rare. However, if found to be in excess of approximately 1%, correction was made by adjustment of the MU setting during the final therapy stage

If the instantaneous midline dose rate for the test irradiation, determined from the quotient of the mid-umbilical dose and the overall test exposure time, differed from the prescribed 7.5 cGy min^{-1}, then an alteration was made to the operating PRF during treatment to restore this rate.

Anthropomorphic phantom. The accuracy of deriving midpoint dose, in the chosen transverse sections, from the measurement of surface dose was investigated using a sectioned anthropomorphic phantom. This part-torso phantom, which was constructed in solid sections of approximate thickness 6 cm, is the result of work undertaken at St Bartholomew's Hospital (White et al, 1981). The anthropomorphic part of the phantom extended from the iliac crest to the clavicles. However, while being used for TBI dosimetric measurements, the total length was increased by the application of additional bolus material at both ends.

Two sections of the phantom (Fig. 7) were made with removable inserts. These were (i) an umbilical section, chosen as it was approximately homogeneous with water and (ii) a mid-thoracic section. Each insert was machined to accept two LiF chips in direct continuity with the tissue substitute material.

The primary role of this phantom in TBI dosimetry is to record transverse dose distribution (this aspect to be reported in a further publication) but initially it was employed to validate the MPD calculation technique. For this purpose the whole phantom was set up to simulate TBI treatment conditions. The TLD chips

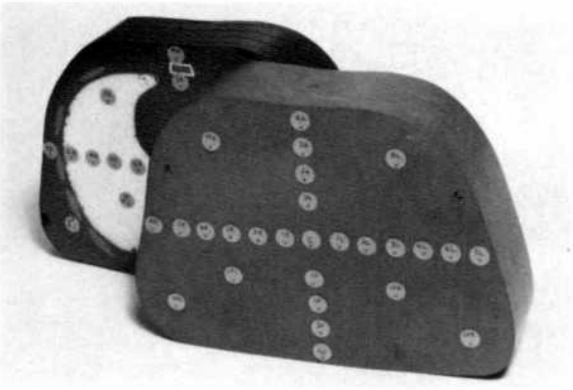

FIG. 7.

Two sections of the anthropomorphic phantom drilled to accept multiple LiF dosemeters.

were loaded into the inserts of both the umbilical and thoracic sections. Sachets containing LiF chips were also placed on the phantom surface in the same manner as described for a patient test irradiation. Irradiations were carried out with the phantom in the supine and decubitus positions.

Computed tomography (CT) (GE 9800 machine) was used to estimate lung density in a small number of patients and in the thoracic section of the anthropomorphic phantom. The patients were scanned in the supine and decubitus positions simulating those of treatment as closely as possible.

Relative density values were calculated for the lung in the areas underlying the position of LiF dosemeters on the chest wall for a series of patients and the phantom. Values of relative electron density (ρ_e) were calculated from the formula

$$\rho_e = 1 + 0.001\ N_{CT}$$

where N_{CT} is the CT number in Hounsfield units between the values -1000 and 100, in accordance with Battista et al (1980).

RESULTS

In this section of the report we aim to quantify the accuracy of our dosimetric approach and to review the dose homogeneity of patients treated to date. Uncertainty limits quoted in measured quantities refer to a 95% confidence interval (± 2 standard deviations) derived by the usual statistical methods.

Accuracy of the TLD technique

Uncertainties associated with the TLD procedure and the ability of the system to measure absolute dose accurately were assessed by considering previous calibration data of individual chips in the batch. The mean change in sensitivity of the batch chips obtained from the batch calibration is used to scale the sensitivities of the remaining chips. However, individual chips in the batch are found to change in sensitivity by amounts differing from the mean, enabling a standard deviation of the mean to be computed. The standard deviations from 20 consecutive batch calibrations were analysed and their standard error calculated to be $\pm 1.7\%$.

When considering the overall accuracy of the procedure the uncertainty associated with the reference ionisation chamber calibration chain must be cumulated with the uncertainty of the TLD system. Planskoy (1983) estimated a total uncertainty (optimal model) in the calibration of a hospital field ionisation chamber of $\pm 1.6\%$ which, when summed in quadrature with the TLD uncertainty, yields an overall uncertainty of $\pm 2.3\%$.

The linearity error associated with the Farmer dosemeter and thimble chambers used has been investigated and found to be negligible (less than $\pm 0.2\%$ over the full range).

Anthropomorphic phantom

The anthropomorphic phantom was used to verify the technique of calculating MPD from measured surface doses; the results are summarised in Table II. Midpoint doses were calculated from mean surface dosemeter readings using the *P* factors in an identical way to that used for actual patients. The relative density of the water substitute section was taken to be 1.00. The electron density of the lung substitute in the mid-thoracic section was found to be 0.25 ± 0.2 from CT scans of the section and this, together with the dimension of the "lung tissue" traversed, was used to compute the effective separation of the section.

TABLE II

COMPARISON OF CALCULATED WITH MEASURED MPDs IN THE ANTHROPOMORPHIC PHANTOM FOLLOWING A SIMULATED TEST IRRADIATION

Phantom section	Separation (cm)	Field	*P* factor	Measured surface dose (cGy)	Calculated MPD (cGy)	Measured MPD (cGy)
"Water"	26	Lateral	0.98	$4.34+0.02$	4.25	$4.21+0.02$
equivalent	18	AP	1.01	$4.52+0.02$	4.57	$4.58+0.03$
Thoracic	26(17)*	Lateral	1.01	$4.80+0.04$	4.85	$5.03+0.02$
$\rho_e = 0.25$	18(12)*	AP	1.01	$4.98+0.03$	5.03	$5.09+0.03$

*Effective separations in parentheses.

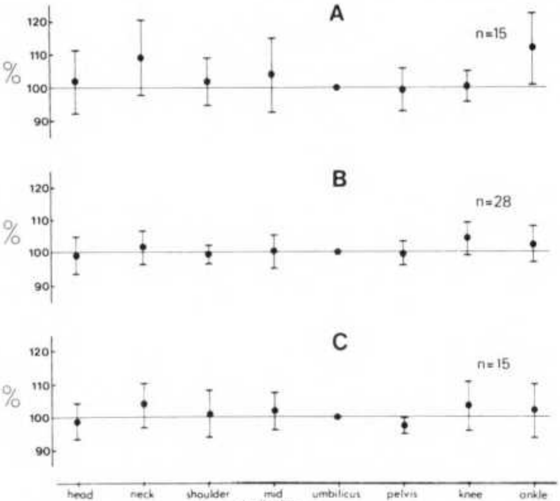

FIG. 8.

Averaged midline doses normalised to the mid-umbilicus for a consecutive series of patients. Children treated using (A) the "early" technique and (B) the "later" technique. (C) Adults treated using the "later" technique. Error bars display ±2 standard deviations from the mean value.

The effective density of the lung substitute compares favourably with the value of 0.28 for the average electron density of healthy adult lung reported by Van Dyk et al (1982). In a series of patients scanned by us so far (all children aged 6–9 years) average electron density was found to be 0.4, somewhat higher than Van Dyk's average for adults.

Patient dosimetry results

In the effort to improve dose homogeneity, the "early" technique was modified to the "later" technique. Using the early technique, 15 children were treated and monitored as described by Fitzgerald et al (1982). From Fig. 8A it is observed that the mean neck dose (including cervical spinal cord) was 10% higher than the mid-umbilical point, and, perhaps of less importance, the mean ankle dose was also this high. The associated standard deviation at all points is seen to be large.

With the "later technique" the following factors were expected to improve the dosimetry: (i) larger field size was available, enabling the patient to lie flat, (ii) accurate tissue bolussing and (iii) the additional flattening filter (*vide supra*). In the "later" technique 28 children were treated and the mean MPD in the eight monitored sections was never in excess of 3% either side of the mid-umbilical dose. Furthermore, the standard deviations are small (Fig. 8B).

In the adult population treated with the "later" technique (Fig. 8C) the largest observed MPD difference in the eight sections monitored was 4% greater than the mid-umbilical dose. The standard deviations were higher than with the child population but the number of patients was small. Nevertheless, it will be seen that the standard deviations and scatter of the means are both lower than in the population of patients treated with the "early technique".

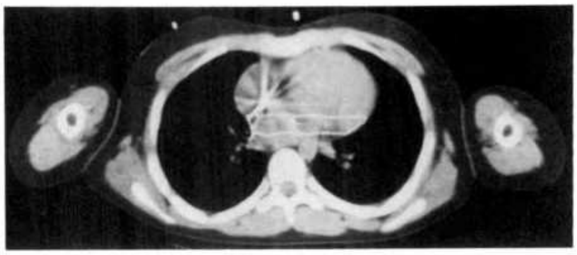

FIG. 9.

Thoracic section CT scan of a patient in the supine TBI position, demonstrating the importance of arm placement in lung "shielding".

Computed tomography

An explicit demonstration of the importance of arm placement can be seen from CT scans of patients in the treatment position (Fig. 9). By judicious placement of the arms it is possible to attenuate the transmitted beam through large volumes of lung. The TLD measurements have shown a substantial dose difference between regions shielded and unshielded in this way. For the series of patients reported here the convention has been, when recording surface doses in the thoracic section, to take measurements from sites not shielded by arms. In so doing it was recognised that maximum mid-axis lung doses would be computed, rather than average or minimum values.

It can also be shown, from CT scans, that gravitational pooling of blood can cause relevant variation in lung density. For example, in one patient positioned in the right decubitus position, the average density of the left lung was found to be 0.31, whereas the right lung had an average density of 0.51. Less significant gravitational density gradients have also been observed in patients scanned in the supine position.

DISCUSSION

Articles describing TBI invariably report the given dosage with respect to a single point. Usually the mid-umbilicus is chosen, but this is not standardised (Barrett, 1982; Shank, 1983). Following consideration of this single point dose it should be emphasised that variation in MPDs along the longitudinal axis of the body will occur; sometimes assumed and quoted as being the maximum and minimum doses throughout the body. This is clearly not so, as dose gradients will also be apparent transversely across the body volume. In this paper, we have concentrated on the study of dosimetry in the longitudinal body axis and on improving midline dose homogeneity. It has been demonstrated that using a medium-energy accelerator with a large field size, together with an additional flattening filter, good dose homogeneity can be achieved. However, there are other considerations that are important in the understanding of TBI dosimetry and in reducing dose gradients within the patient.

If parallel opposed fields are used exclusively, for example bilateral fields, not only will this result in a dose gradient along the beam axis in any given section but also orthogonal to it as the patient shape changes anteriorly and posteriorly (Svensson et al, 1980; Van Dyk, 1983). These gradients are reduced if exceptionally long SSDs and high beam energies are utilised, such as the technique reported by Goolden et al (1983). Alternatively, in an attempt to improve dose uniformity, four fields (bilateral, anterior and posterior) can be used. This provides the additional advantage of using different treatment positions together with the ability to optimise beam weighting, in an effort to minimise longitudinal MPD gradient.

In order to ensure optimum dose homogeneity, it is necessary to have some facility to compensate for tissue deficits within transverse body sections and between one body section and another. Two methods were considered: remote compensation or appositional tissue bolus. The former method was rejected in that it places too severe a requirement on correct alignment of the patient with the compensator mounted in the treatment head at large TBI treatment distances. Moreover, the acknowledged advantage of remote tissue compensation over bolus, *i.e.* the preservation of skin sparing, was considered undesirable for TBI leukaemic patients.

The bolus material used in skin apposition was well tolerated by the patients. The position and quantity used for each patient was fully documented at the time of testing. Being essentially solid and packed in non-slip polyurethane bags the bolus material provided additional stability and reproducibility to the patient's position. As the malleable material can be pressed into slabs of uniform thickness it is possible to change the quantity used on an individual patient in the event of an unacceptable dose distribution. If, for example, the midpoint neck dose is found to be too high at the test irradiation, then the thickness of bolus would be increased for the treatment session. A calculation method by which the change in the thickness of bolus that is necessary to correct the MPD to an acceptable level has been devised

Since leukaemic cells may be present in those regions of the skin afforded blood supply, it is essential to treat even superficial layers of the patient to high dose—hence the perspex screen. It is obviously important to quantify these doses but particularly so when entrance and exit measurements are used to predict internal doses. The surface LiF dosemeters must be used under conditions where electron equilibrium is established or at least where the electron fluence is not changing rapidly. These conditions were shown to exist by the entrance- and exit-dose studies.

From the results of the test irradiation, the field weightings producing the optimum dose distribution have been computed for each patient. The computer program developed at St Bartholomew's Hospital will allow subjective bias to be inserted into the calculation. For example, the importance of dose homogeneity in the lower legs relative to the umbilicus may be considered to be less relevant than homogeneity in the thoracic sections. Previous clinical history might predispose some region of a particular patient to increased sensitivity to high or low doses. If uniform significance is given to each section, then the optimum field weighting based simply on mathematics may in practice not produce the most satisfactory distribution for an individual patient. Use of "significance factors" allows the operator to inject an element of subjective trimming for a particular patient or clinical situation. In general this results in an alternative distribution for consideration alongside the uniformly weighted best. The choice of which of these, or indeed any other combination of field weightings, to use for treatment was made by the clinician.

When our TBI procedure was initiated, early lack of confidence in a single test irradiation promoted the practice of a second dose measurement taken during the first 10% phase of the therapy session. Inevitably, differences in the dose distribution calculated from the test compared with the first stages of the treatment irradiation were observed. These small differences were attributed to variation in patient position between the treatment and test. Neither assessment was necessarily more valid as a final determination, since several more changes of patient position were involved. The problem was circumvented by placing greater emphasis on reproducing exactly the patient's tested position. The procedure of making a second complete test was then discontinued.

Throughout the test and treatment sessions additional machine output monitoring is recommended as an independent check for constancy and linearity. The output (cGy per MU) must be stable between the test and treatment procedures. Other benefits of this monitoring include the detection of erroneous MU setting, misplacement of the perspex screen or additional flattening filter, and non-linearity of the integral machine dosimetry system during the treatment session.

The actual role of radiation in the multifactorial pathogenesis of infective or idiopathic interstitial pneumonitis (IPP) is not known. However, an association of the idiopathic variety with TBI is generally acknowledged. Studies from many centres (Keane et al, 1981; Van Dyk et al, 1981; Cardozo et al, 1985; Kim et al, 1985) have demonstrated both a dose and dose-rate relationship with IPP. It is essential to determine accurately the absolute absorbed dose in the thoracic region.

A method suggested by Van Dyk et al (1981), that of calculating lung dose using equivalent tissue–air ratios, requires comprehensive CT scanning of each patient. The option reported here of determining lung MPD from surface measurements, while lacking spatial resolution, is considered to be accurate on a point basis. Acceptable resolution can be obtained by using multiple measurement sites. The effect of tissue inhomogeneity is implicitly accounted for when using transmission data to calculate MPDs. When assigning *P* factors related to the effective separation, inaccuracies will ensue in the absence of actual lung density values; however, at 6 MV energy the *P* factor function for typical thoracic section separations shows minimal variation. Therefore, we believe that the calculation of mid-thoracic doses from multiple-site surface-dose measurements circumvents the need for individual CT-based isodosimetry on all patients undergoing TBI.

In conclusion, we have described a technique for TBI which produces good dose homogeneity throughout the patient and is achieved with a standard linear accelerator in an orthodox-sized treatment room. The methods of dosimetric monitoring have been discussed with regard to their relevance to confirming the objectives of this study.

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The implications of *in-vitro* radiation–survival curves for the optimal scheduling of total-body irradiation with bone marrow rescue in the treatment of leukaemia

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ABSTRACT

A mathematical model for optimal scheduling of total-body irradiation (TBI) in the treatment of leukaemia is described. A survey of the radiosensitivities of human leukaemic cells indicate that they are highly radiosensitive with little fraction size dependence (median $D_0 = 0.74$ Gy; median $D_q = 0.14$ Gy). These properties, when considered alongside the high repair capacity of lung, suggest that TBI schedules of the "accelerated hyperfractionation" type are optimal. The antileukaemic effects of alternative schedules, chosen to be isoeffective for lung damage to a reference schedule of 6 × 2 Gy in 3 days, were compared. A modestly hyperfractionated schedule of 10 fractions of 1.3–1.5 Gy in 5 days has theoretical advantages while retaining practicality of clinical administration.

Following total-body irradiation (TBI) and bone marrow transplantation, leukaemic recurrence remains a problem (Deeg et al, 1984). The major constraint on the radiation dose is imposed by the limited ability of non-transplantable normal organs to withstand radiation damage. In practice, radiation pneumonitis represents the main constraint (Keane et al, 1981).

Alterations to the fraction size could lead to a useful increase in radiation dose by exploiting the differences in repair characteristics between leukaemic cells and normal lung (Peters et al, 1979). We have used a mathematical model to simulate the effects of a number of theoretical schedules on a leukaemic cell population. The common characteristic of the schedules is that they are isoeffective for lung. They represent the degree of late lung damage expected with a "reference schedule" which is commonly used in practice. The radiobiological parameters of the leukaemic cell population are derived from *in-vitro* studies.

IN-VITRO RADIOSENSITIVITY OF HUMAN LEUKAEMIC CELLS

We have surveyed the literature on the *in-vitro* radiosensitivity of human leukaemia cells. A total of 11 sets of measurements were made on eight different established cell lines and 22 sets of measurements were carried out on leukaemic progenitor cells from either bone marrow aspirates or peripheral blood from a total of 20 different patients. Of these, there were 24 of myeloid origin, three of lymphoid origin and one erythroleukaemia. The cell-survival parameters are expressed by values of D_0 and D_q and are shown in Table I. D_0 corresponds to the reciprocal slope of the straight-line portion of the cell-survival curve, where it is the dose required to reduce the proportion of clonogenic cells by a factor e^{-1} (0.37). D_q corresponds to the width of the "shoulder" on the cell-survival curve. It is the dose value where the back-extrapolation of the straight-line portion of the curve intersects the dose axis. There is some heterogeneity in the sets of measurements but the majority are of small values of both D_0 and D_q. No difference in radiosensitivity is apparent between the cells of myeloid origin and the others. For this reason they are considered together. The median value of D_0 is 0.74 Gy and the median value of D_q is 0.14 Gy. These parameters indicate that leukaemic cells are highly radiosensitive with a low capacity for the accumulation and repair of sublethal damage.

MATHEMATICAL MODEL

The purpose of the model studies was to answer the following question: given the best available estimates of the radiosensitivity of leukaemic cells and an accurate isoeffect model for lung, what schedules appear most appropriate for the treatment of leukaemia by TBI? The fractionated "Seattle schedule" of six fractions of 2 Gy, twice daily over 3 days, which is presently used clinically (Clift et al, 1982) and which is considered to carry an acceptable risk of pneumonitis, is adopted as a reference schedule. All other schedules were chosen to give equivalent levels of lung damage to the reference schedule.

The mathematical details of the model will be presented elsewhere. The principal radiobiological assumptions are as follows:

(1) The multitarget equation is used to describe the sterilising effect of radiation on leukaemic cells. This equation underestimates the effect of small doses. However, the affected region for typical leukaemia cells is small and errors will be insignificant at clinically relevant fraction sizes.

TABLE I

THE RADIATION-SURVIVAL CURVE PARAMETERS FOR LEUKAEMIC CELLS GROWN *IN-VITRO*

Designation	Type	D_0/Gy	D_q/Gy	n	Source
1	AMML	2.10	0.55	1.3	Ozawa et al (1983)
2	APL	1.88	0.18	1.1	Ozawa et al (1983)
3	AMML	1.88	0.63	1.4	Ozawa et al (1983)
4	AMML	1.23	0.32	1.3	Ozawa et al (1983)
5	AML	1.35	0.35	1.3	Ozawa et al (1983)
6	AML	1.20	0.31	1.3	Ozawa et al (1983)
7	AML	0.90	0.16	1.2	Ozawa et al (1983)
8	AMML	0.70	0.13	1.2	Ozawa et al (1983)
9	AMML	0.70	0.07	1.1	Ozawa et al (1983)
10	AMML	0.55	0.00	1.0	Ozawa et al (1983)
11	AML	0.50	0.00	1.0	Ozawa et al (1983)
12	AML	0.30	0.00	1.0	Ozawa et al (1983)
176	acute monomyelogenous leukaemia	0.76	1.05	4.0	Weichselbaum et al (1981)
CS	ANL (BM cells)	0.57	0.00	0.92	Kimler et al (1985)
GH	ANL (BM cells)	0.51	0.00	0.95	Kimler et al (1985)
JR	ANL (BM cells)	0.68	0.00	0.92	Kimler et al (1985)
TL	ANL (BM cells)	0.68	0.00	1.01	Kimler et al (1985)
GS	ANL (BM cells)	0.72	0.00	0.84	Kimler et al (1985)
HF	ANL (BM cells)	0.56	0.00	1.11	Kimler et al (1985)
JL	ANL (BM cells)	0.48	0.03	1.07	Kimler et al (1985)
LJ	ANL (BM cells)	0.95	0.24	1.29	Kimler et al (1985)
U937	histiocytic/monocytic leukaemia	0.88	1.34	4.6	Fitzgerald et al (1986)
KG1	monomyeloid leukaemia	0.84	0.62	2.08	Fitzgerald et al (1986)
HL60	monomyeloid leukaemia	1.22	0.66	1.8	Mean of Fitzgerald et al (1986) and Weichselbaum et al (1981)
JY	B-cell lymphoma	0.61	0.40	2.13	Fitzgerald et al (1986)
Daudi	B-cell lymphoma	0.57	0.13	1.25	Fitzgerald et al (1986)
K45	T-cell ALL	1.05	0.07	1.05	Mean of Fitzgerald et al (1986) and Weichselbaum et al (1981)
K562	erythroleukaemia	1.52	0.52	1.4	Mean of Fitzgerald et al (1986) and Weichselbaum et al (1981)

AMML = acute myelomonocytic leukaemia, APL = acute promyelocytic leukaemia, AML = acute myeloblastic leukaemia, ANL = acute non-lymphocytic leukaemia, BM = bone marrow, ALL = acute lymphocytic leukaemia

The median parameter values for the data are median D_0 = 0.74 Gy and median D_q = 0.14 Gy.

(2) Lung is taken to be the dose-limiting tissue and the fractionation schedule in lung to be of paramount importance. The leukaemic cell population throughout the body is assumed to receive a uniform dose equal to that received by lung. In practice this would require the use of a compensator for the reduced density of lung.

(3) Radiation damage to lung is adequately described by the well known quadratic model (Barendsen, 1982; Thames et al, 1982; Fowler, 1984) with $\alpha/\beta = 3$ Gy (Parkins & Fowler, 1985).

(4) Repair of radiation damage in the lung is completed in the time between fractions. Evidence suggests that at least 6 h may be necessary to achieve this (Vegnesa et al, 1985) and it is assumed in the analysis that there is at least 6 h between fractions.

(5) Leukaemic cell radiosensitivity is given by the median parameters of Table I. A growing body of work has suggested that *in-vitro* radiosensitivity data are closely related to tumour radiosensitivity in the clinic (Fertil & Malaise, 1981; Deacon et al, 1984; Fertil & Malaise, 1985). It is possible, therefore, that these data will lead to clinically applicable conclusions. It is assumed that leukaemic cells proliferate exponentially between fractions.

(6) Radiation is given at a high dose rate (so that variations in dose rate will be of little relevance radiobiologically).

OPTIMAL SCHEDULING OF TBI

The antileukaemic effects of a variety of schedules, isoeffective for lung damage to the reference schedule, were calculated. Up to a maximum of four fractions per day could be given, consistent with the requirement for 6 h between fractions. Figure 1 plots leukaemic log cell-kill against fraction size for schedules of two fractions

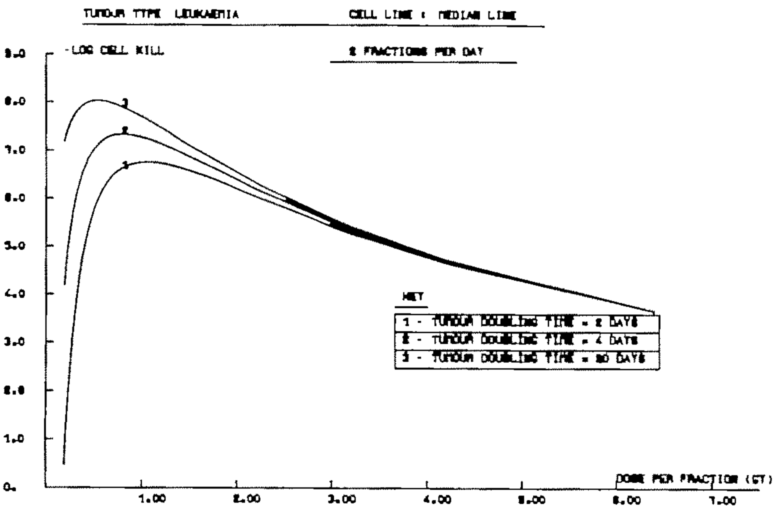

FIG. 1.

Leukaemic log cell-kill as a function of dose per fraction for radiotherapy schedules of two fractions per day, isoeffective to 6 × 2 Gy on the basis of the quadratic model with $\alpha/\beta = 3$ Gy. Leukaemic radiosensitivity is given by the median parameters of Table I

per day. When moving from large to small fractions, there is first an increase in therapeutic effect as advantage is taken of the different radiobiological parameters of lung and leukaemic cells, until a maximum neoplastic cell-kill is reached. This applies for all doubling times considered. Thereafter the effect on leukaemic cells decreases owing to the effects of proliferation. Figure 2 shows the relationship between the fraction size of the optimal schedule, the number of daily fractions and the growth rate of the leukaemic cell population. The log cell-kills produced by the optimal schedules are plotted in Fig. 3.

The effect of a single fraction of 7.5 Gy (Song et al, 1981) has been included for illustrative purposes. A dose of this size, given at a high dose rate, probably represents the upper limit of acceptability from the point of view of induction of pneumonitis (Van Dyk et al, 1981). Doses of up to 10 Gy have, however, been given at moderate to low dose rates. The toxicities produced by these schedules are highly dependent on the specific dose rate but usually exceed that produced by six fractions of 2 Gy. Schedules of this sort are not considered in this paper, which is concerned with taking a certain level of toxicity and finding the optimal

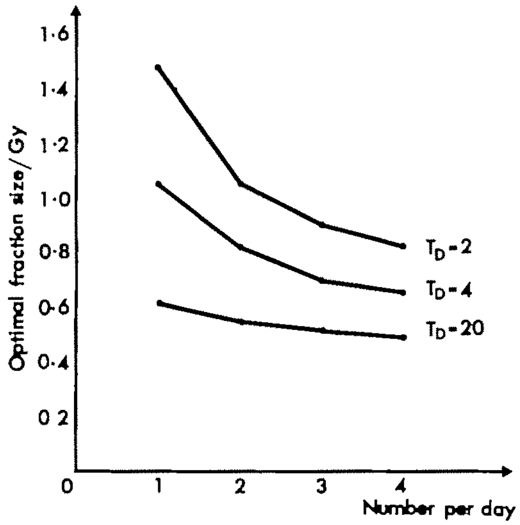

FIG. 2

The optimal dose per fraction as a function of the number of daily fractions for three different values of leukaemic doubling time. All schedules are isoeffective for lung to six fractions of 2 Gy (quadratic model: $\alpha/\beta = 3$ Gy).

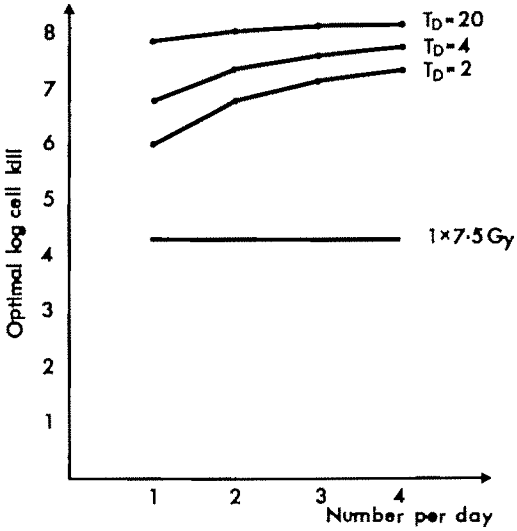

FIG 3.

The leukaemic log cell-kill produced by the optimal schedules as a function of the number of daily fractions for three different leukaemic doubling times.

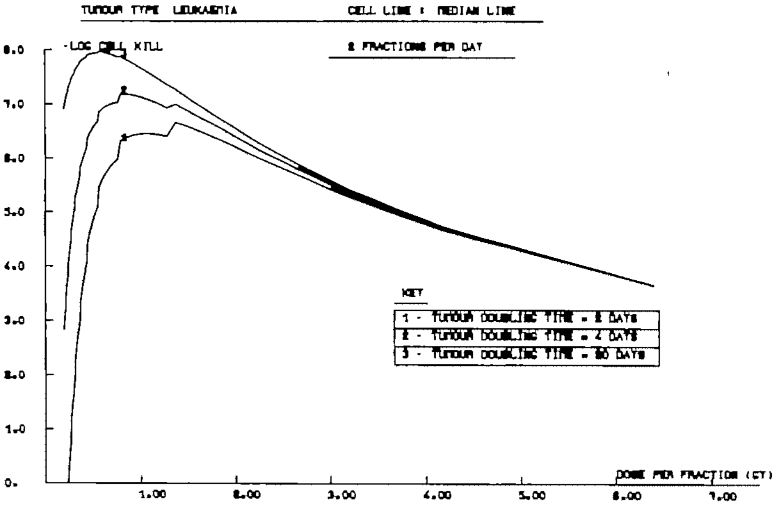

FIG. 4.

Leukaemic log cell-kill as a function of dose per fraction for radiotherapy schedules of two fractions per day with no treatment over weekends. Schedules are isoeffective to six fractions of 2 Gy on the basis of the quadratic model with $\alpha/\beta = 3$ Gy. Leukaemic radiosensitivity is given by the median parameters of Table I.

schedule consistent with it. The theoretical comparison of continuous low dose rate exposures and fractionated TBI is complex and is dealt with in detail elsewhere (O'Donoghue, 1986).

DISCUSSION

It is possible to make some general observations on the optimal schedules deduced from the model computations (Fig. 2). The fraction size of the optimal schedule is dependent on the leukaemic doubling time and also on the number of fractions which are given per day. For longer leukaemic doubling times the duration of the schedules is less critical and there is less variation in the optimal schedules for different numbers of daily fractions.

Figure 3 shows the log cell-kills produced by the optimal schedules. It can be seen that the shorter the leukaemic doubling time the more advantage there is in delivering more fractions per day. There is a greater advantage in going from one fraction per day to two fractions per day than there is in going from two to three fractions per day, which in turn has a greater advantage than going from three to four fractions per day. The effect of a single fraction of 7.5 Gy has also been shown. Although, by the quadratic model, this schedule is more damaging to lung than the others, the effect on the leukaemic cell population is rather less.

We now wish to consider schedules which are practically achievable, to see if there is a realistic prospect for an improvement in treatment. The criteria we have taken for practicality are that treatment must take place within normal working hours, *i.e.* 9 a.m. to 5 p.m., and that there will be no treatment over weekends.

These criteria rule out schedules of three and four fractions per day when taken along with the requirement for at least 6 h between fractions. As schedules of two fractions per day are always better than those of one fraction per day, we restrict our attention to schedules of two fractions per day with no treatment over weekends. This situation is represented in Fig. 4. Weekend breaks in treatment correspond to the discontinuities in the plots. It can be seen that the schedule of 10 fractions of 1.37 Gy is close to the optimal for doubling times of 2 days and 4 days. For longer doubling times, *e.g.* 20 days, the effectiveness continues to increase with decreasing fraction size. Doubling times of 2–4 days are thought to be more appropriate for leukaemias (Steel, 1977). Hence a schedule consisting of 10 fractions (twice daily) of 1.37 Gy provides an "optimal" regime which is readily achievable in practice. The "accelerated hyperfractionation" structure of the schedule (Thames et al, 1983) is what might be expected for a fast-growing neoplasm with low repair capacity whose treatment is limited by the tolerance of a late-responding normal organ with high repair capacity.

CONCLUSIONS

The precise numerical value of 10 fractions of 1.37 Gy as optimal schedule is dependent on the level of acceptable normal-tissue damage as set by the reference schedule and also on the repair capacity of lung. These factors are subject to uncertainties due to radiation dosimetry and interpatient variability, which may be expected to blur the optimal schedule. Bearing this in mind, our conclusions may be summarised as follows. For the median values of leukaemic radiosensitivity found in the survey, "accelerated hyperfractionation" appears optimal. It seems clear that single fractions at a high dose rate are inappropriate. We suggest that a practical schedule of 10 fractions of between 1.3 Gy and 1.5 Gy in 5 days is worth considering for the treatment of leukaemia and should be tested clinically.

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Book reviews

Differential Diagnosis in Pediatric Radiology. By Michael Grunebaum, pp. 139, 1986 (S. Karger AG, Basel), £19 50.
ISBN 3–8055–4249–6

This small book, conveniently fitting into a coat pocket, consists of over 400 lists of radiological signs. These are grouped into six systems, respiratory, cardiovascular, urinary, gastrointestinal, skeletal, and head. There are, in addition, some lists of major clinical signs. In each system the lists refer first to the newborn period, with infancy and childhood in the later parts of the section. There are 10 pages of general references and an adequate index.

Each particular clinical or radiographic sign is followed by a list arranged in alphabetical order rather than in frequency of appearance. The lists of differential diagnoses are generally comprehensive.

The book will provide a memory aid and a useful source of information to those in training. The lack of further evaluation of each possible diagnosis, although impractical in a book this size, would usually mean recourse to more comprehensive textbooks, especially in the case of bone dysplasias and some obscure syndromes.

There are some scattered typographical errors but the context is generally reasonable, although "medullary sponge kidney" giving rise to a gamut of calyceal diverticula, nephrocalcinosis, renal papillary necrosis and renal tubular acidosis might well be considered contentious. This form of text is a matter of personal preference; at over £19 one would need to peruse the book personally before buying.

D. G Shaw

Diagnosis of Metabolic Bone Disease. By P. Grech, T. J. Martin, N. A. Barrington and P. J. Ell, pp. viii+364 +references+index, 1985 (Chapman & Hall Medical, London), £40.00.
ISBN 0–412–26580–X

Metabolic bone disease is a topic which has sometimes been neglected in radiological texts of the skeleton, so to have a book devoted to this subject is welcome. The authors are largely British, drawn principally from Sheffield, with the clinical contribution being from an Australian physician.

The book begins with a fairly detailed introduction to bone composition and physiology, hormones which influence calcium metabolism and the technique for bone biopsy The histological changes seen in various metabolic bone diseases are described and quantitative histo-morphometric measurements are included Methods available for assessing skeletal maturation and for making quantitative measurement of bone mass are discussed. The principal radiological and biochemical features of osteoporosis, rickets and osteomalacia and conditions which result in osteosclerosis are described initially. Subsequent chapters are allocated to the bone diseases associated with endocrine, renal and gastrointestinal disorders, those induced by drugs or tumours and those associated with calcification or ossification at sites outside the skeleton. This format leads to some repetition in the text. The authors have included a wide variety of conditions, such as Paget's disease and sarcoidosis, which are not strictly examples of "metabolic" bone disease but, nonetheless, have interesting radiological appearances and are important among differential diagnoses to be considered. This is legitimate and desirable, but there is an over-emphasis on these conditions at the expense of more detailed consideration of truly "metabolic" bone diseases, particularly those that are uncommon but of relevance to readers interested in this field. Each chapter, however, is accompanied by a substantial number of useful and pertinent references. The last chapter is devoted exclusively to the principles, application and pathological appearances of radionuclide bone scans in a wide variety of bone disorders.

The illustrations are of reasonable quality, although in some the more subtle changes (*i.e.* subperiosteal erosions) are not easily seen. Quite long legends are given with some of the illustrations and the printing layout, with the text occupying a column only two-thirds of the width of the page, results in many pages being incompletely filled.

Although this is not, and is not intended to be, a definitive reference book, the authors have produced a useful introduction to the subject. They succeed in their aim, showing how radiological and biochemical approaches contribute to diagnosis and the book would certainly be useful to radiologists, particularly during their more senior years of training, and to junior clinicians who have to manage patients with metabolic bone disease. It is modestly priced and good value for money.

J. E. Adams

Measurement of the Performance Characteristics of Diagnostic X-ray Systems Used in Medicine. Part V. Conventional Tomographic Equipment. Hospital Physicists' Association, pp. 20, 1985 (HPA, London), £6.00.
ISBN 0–904181–35–9

This booklet is fifth in a series dealing with the measurement of performance of diagnostic X-ray systems. It covers those aspects of performance which are specific to conventional tomographic equipment, namely the position, orientation and thickness of the cut "plane" and assessment of the tomographic movement. Spatial resolution and the performance of masking and coning devices are also included, but more general topics such as X-ray tubes, films and screens are dealt with in other reports in the series.

In six tersely written pages the relevant aspects of performance are introduced, appropriate test objects are described and test procedures are outlined. Sample data sheets and a selection of measurements made on 20 tomographic systems are given in appendices and there is a short but useful list of references. The publication is well produced with clear print on A4-size pages There are some minor blemishes: in the first sentence of Section 1.4 the word "equipment" should presumably be "performance", some of the dashed lines in Figure 2 could be clearer; there are a few trivial misprints.

As a practical guide to the assessment of performance of tomographic equipment it should prove to be a useful booklet, since it provides a succinct summary of important concepts together with clear directions for carrying out a range of basic tests. It does not aim to provide the comprehensive coverage which might be required by a physicist or engineer engaged in research or development in this field.

G. P. Lawrence

1987, *The British Journal of Radiology*, 60, 285–286 MARCH 1987

Case reports

A tumour-like bone lesion as a manifestation of vitamin D-resistant hypophosphataemic osteomalacia

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In 1959 Prader et al described for the first time an association of vitamin D-resistant hypophosphataemic rickets with a giant-cell granuloma. Removal of this tumour, located in a rib, led to complete healing of the rickets. Since then such tumours, usually of mesenchymatous origin, have been found in a number of patients with rickets or osteomalacia and the condition has become known under various names such as tumour rickets, oncogenic rickets and tumour-induced hypophosphataemic rickets (or osteomalacia, when it occurs in adults) (Ryan & Reiss, 1984). This condition should be distinguished from X-linked or congenital hypophosphataemic vitamin D-resistant rickets. Marked hypophosphataemia resulting from reduced renal tubular reabsorption of phosphate is the common finding in both conditions and although there are clinical differences between them the diagnosis can sometimes be difficult.

Here we describe a patient with congenital hypophosphataemic rickets and a bone lesion which had all the radiological features of a tumour but which proved to be a secondary feature of the disease.

CASE REPORT

A 19-year-old girl was found at the age of 4 years to have congenital hypophosphataemic rickets. She was treated up to the age of 17 years with various vitamin D preparations including vitamin D_2, dihydrotachysterol, 1α-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol either alone or in combination with oral phosphate. Details of these therapeutic regimes have been published previously (Bueller et al, 1982). In short, during the early years of life treatment had been irregular, with subsequent development of severe deformities of the legs requiring repeated surgical corrections, the last one at the age of 14.9 years. At that time the rachitic process was well controlled with 1,25-dihydroxycholecalciferol (1 to 2 μg/day) and oral phosphate. However, because of a rise in serum calcium, the dose of 1,25-dihydroxycholecalciferol was reduced and all medications were eventually discontinued at the age of 17 years. Subsequently, the serum calcium remained elevated and the serum phosphate decreased to values around 0.4 mmol/l.

Pain occurred in the right leg at the age of 18.8 years and radiographs revealed a fracture of the distal right femur, without displacement, which had the appearance of a Looser's zone (wide, linear, translucent zone across the shaft). Treatment consisted of bed-rest with suspension of the leg, but there was no improvement. A radiograph of the hands revealed a localised area of bone resorption with interruption of the cortex and elevation of the periosteum in the midshaft of the second metacarpal of the right hand (Fig. 1A). Subperiosteal erosions were not seen. This appearance was compatible with a bone tumour, and independent assessment by two experienced radiologists led to the same conclusion. Biopsy of the lesion showed no evidence of malignancy and the specimen (decalcified) consisted of lamellar and non-lamellar bone with some fibrotic changes.

The patient had hypophosphataemia (0.42 mmol/l) as a result of reduced renal tubular reabsorption of phosphate (TmP/GFR 0.25 mmol/l), a slightly elevated serum calcium level (2.56 mmol/l) and a high serum alkaline phosphatase level (204 U/l; normal <60). Repeated measurements of serum parathyroid hormone (PTH) with antisera of different antigenicity revealed normal or suppressed values and circulating concentrations of vitamin D metabolites were within the normal range. A skeletal survey showed a fracture of the right fibula in addition to the known fracture of the femur and the lesion of the hand. An undecalcified iliac crest biopsy showed markedly increased osteoid with no evidence of increased bone turnover or marrow fibrosis. As malignancy and hyperparathyroidism had been excluded, it was thought that the lesion was a secondary feature of the disease and it was decided to treat the patient with oral phosphate. After 2 months there were already signs of mineralisation of the metacarpal bone lesion (Fig. 1B). Serum calcium had become normal and at this stage 1,25-dihydroxycholecalciferol (3 μg/day) was added to the treatment. A further decrease of serum calcium was observed, indicating that the initial elevation was probably due to inability of bone to utilise calcium for mineralisation. After a further 2 months, the bone lesion had greatly improved (Fig. 1C) and the fractures of the femur and the fibula had been repaired. Nine months after starting therapy, complete healing was seen (Fig. 1D).

DISCUSSION

The presence of a tumour-like bone lesion in a patient with hypophosphataemia and osteomalacia is strongly suggestive of tumour-induced osteomalacia. The course of events in the patient reported here, however, confirmed that this picture can be an unusual radiological manifestation of osteomalacia which, to our knowledge, has not been previously described. The diagnosis of tumour-osteomalacia was already unlikely on clinical grounds since this does not present in early childhood, although it may run a long course before it

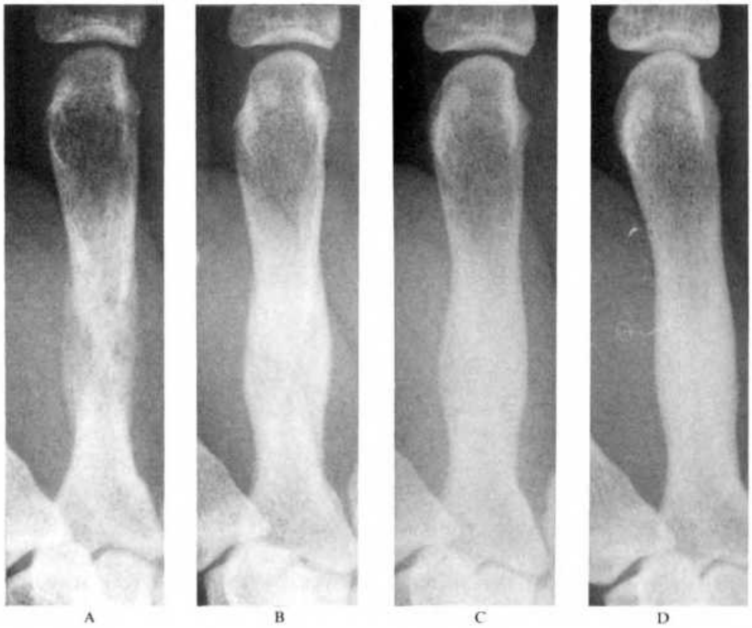

FIG. 1.

Sequential X-rays of the second right metacarpal bone (A) before treatment; (B) after 2 months' treatment with phosphate; (C) and (D) after treatment with phosphate and 1,25-dihydroxycholecalciferol for 2 months and 7 months, respectively.

is discovered. In addition, its clinical picture is characterised by muscle weakness, a feature which is not encountered in patients with congenital or X-linked hypophosphataemia. Final proof came from the biopsy of the metacarpal lesion which showed no evidence of a tumour.

Another possibility was that the lesion represented an atypical brown tumour, since hyperparathyroidism can develop in patients with hypophosphataemic rickets after treatment with phosphate (Firth et al, 1985). This could be further supported by the high serum calcium concentrations found. The serum PTH level, however, was normal, and there were no other radiological signs or histological features of hyperparathyroid bone disease. The therapeutic response to vitamin D and oral phosphate supplements was finally conclusive.

The reason why bone destruction can occur in this manner is not clear, but the pathogenesis may be analogous to the development of Looser's zones or pseudofractures in general. These consist of reactive fibrous tissue in which non-lamellar bone can be found and they can be considered characteristic of osteomalacia of any type (Byers, 1977). They may occur following microfractures caused by local stress or trauma. The radiographic appearance resembling callus formation in our patient is compatible with this view. Since osteomalacia may develop insidiously, it is possible that such a lesion may also be the first sign of the disease and careful evaluation of all available data is necessary before a final diagnosis is made and appropriate treatment instituted.

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1987, *The British Journal of Radiology*, 60, 287–288

Case reports

Superior mesenteric artery aneurysm diagnosed by ultrasound

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Superior mesenteric artery (SMA) trunk aneurysms are very uncommon. The last reported incidence was one in 12 000 consecutive autopsies (Lucke & Rea, 1921). Aneurysms of its branches are also rare; as far as we are aware, only 40 cases have been mentioned in the literature up to 1980.

A case of an aneurysm of the superior mesenteric artery trunk suggested by real-time ultrasound and confirmed by angiography is presented. To our knowledge this is the first case published in which the diagnosis was reached by ultrasound and fine-needle aspiration.

CASE REPORT

An 87-year-old white woman presented in the casualty department with sudden onset of abdominal pain and bilious vomiting. On examination, the pulse was 106/min and blood pressure 100/60 mm Hg. The abdomen was soft but there was tenderness and a vague swelling in the left iliac fossa. All the peripheral arterial pulses were palpable.

On admission, the serum amylase level was elevated to 8620 IT/l. The serum sodium level was 137 mmol/l, potassium level 2.8 mmol/l, chloride level 97 mmol/l, bicarbonate level 24.7 mmol/l and urea level 4.5 mmol/l.

In spite of normal abdominal ultrasonic findings, symptomatic treatment for acute pancreatitis was initiated. The abdominal pain and raised serum amylase persisted during the next week and a pyrexia of 37.8°C developed.

A second ultrasound examination on the third day after admission confirmed the presence of a normal pancreas and aorta. The liver, gallbladder, and spleen were also normal. However, the examination of the lower abdomen now revealed the presence of a 6 cm rounded mass, deep in the left iliac fossa. This lesion showed predominantly medium- and low-level echoes surrounding a central round anechoic area (Fig. 1). No pulsation of this mass was observed on the real-time examination, and for further investigation it was punctured under ultrasound guidance, using a 20G spinal needle, resulting in the aspiration of 30 ml of arterial blood. During this procedure the mass was seen to be moving freely from the left to the right of the midline.

A superior mesenteric artery aneurysm was suggested and confirmed at subsequent angiography (Fig. 2).

At laparotomy, oedema of the pancreas adjacent to the aneurysm was noted but no obvious complications from the needle aspiration were observed. The aneurysm was successfully excised, but a pancreatic duct was inadvertently injured during dissection. Post-operatively, the patient developed a transient pancreatic fistula, but despite this, continued to make steady progress. Unfortunately, she died suddenly in the fifth post-operative week from a pulmonary embolus.

DISCUSSION

Elective surgery is recommended in SMA aneurysms, as complications and mortality rate increase in emergency operation, and therefore pre-operative demonstration of SMA aneurysm is important, as surgical exploration alone, without previous radiological studies, often fails to identify the anatomical origin of the aneurysm (Carter & Gosney, 1966; Kleinsasser, 1970). Arteriography is the traditional mode of demonstrating SMA aneurysm; unfortunately this is rather an expensive and invasive procedure.

In recent years, non-invasive modalities such as radionuclide hepatic blood-flow imaging have been effective in the diagnosis of abdominal aortic (Bergen et al, 1974) and hepatic artery (Sukerkar et al, 1977) aneurysms. Edwin et al in 1972 also demonstrated an

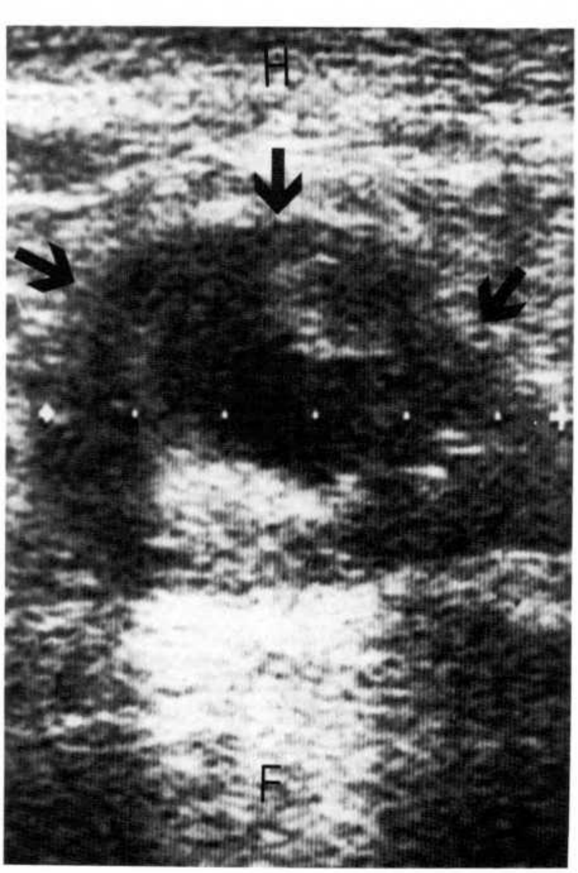

FIG. 1.

Real-time ultrasound scan showing a 6 cm, low-echogenic mass (arrows) with a round central anechoic area.

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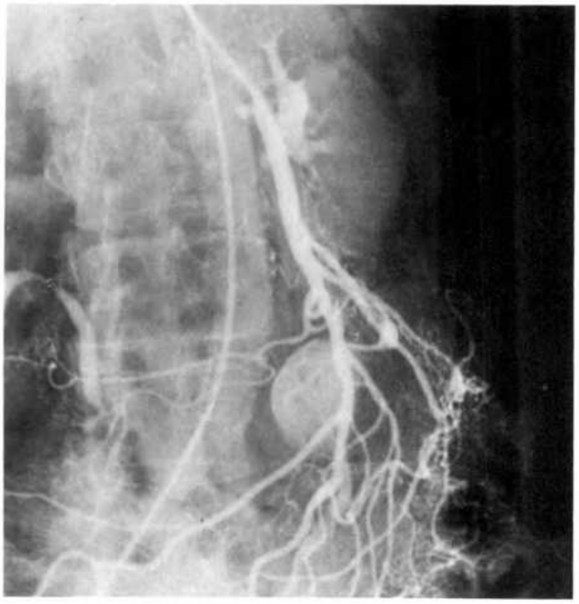

FIG. 2.

The aneurysm fills from the superior mesenteric artery displacing adjacent vessels showing the real size of the lesion.

abdominal focal blush of activity in the region of the SMA at arteriography.

In our case, real-time ultrasound suggested an aneurysm of the SMA, *i.e.* the presence of a mobile mass with ultrasonic characteristics of an aneurysm in the region of the mesenteric arteries. It did not, of course, exclude an aneurysm of other visceral arteries such as the inferior mesenteric artery, which although rare could present similar characteristics. Although an aneurysm was suspected it is, nevertheless, a rare condition and it was felt justifiable first to perform fine-needle aspiration before embarking upon the more invasive and time-consuming procedure of angiography.

Although arteriography will always be necessary pre-operatively, early recognition of this abnormality using a non-invasive modality like ultrasound will result in considerable saving of time and resources in the investigation of such an unusual condition.

ACKNOWLEDGMENTS

We wish to thank Mr G. Lord, Consultant Surgeon, for referring this patient for radiological examination and for access to clinical details.

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Dysplasia epiphysealis hemimelica of the ulna

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Dysplasia epiphysealis hemimelica is a developmental disorder of childhood in which there is a symmetrical cartilaginous overgrowth of one or more epiphyses or of a tarsal or carpal bone. The disorder is usually limited to the medial or lateral half of a single extremity and the lesion is microscopically indistinguishable from an osteocartilaginous exostosis. The disorder was first described and called tarsomegaly by Mouchet and Belot in 1926. The purpose of this paper is to report a patient in which the disease involves the ulna. This is very rare.

CASE REPORT

A girl aged 6 years was brought for consultation because of a swelling over the ulnar aspect of the right wrist without any pain or limitation of movement of the wrist.

X-ray examination showed a very enlarged lower ulnar epiphysis (Fig. 1). The height of the distal ulnar epiphysis was twice that of the distal radial epiphysis and the width of the epiphysis overlapped that of the ulnar diaphysis. The metaphysis was dense and somewhat irregular and the right ulna was slightly shorter than the left.

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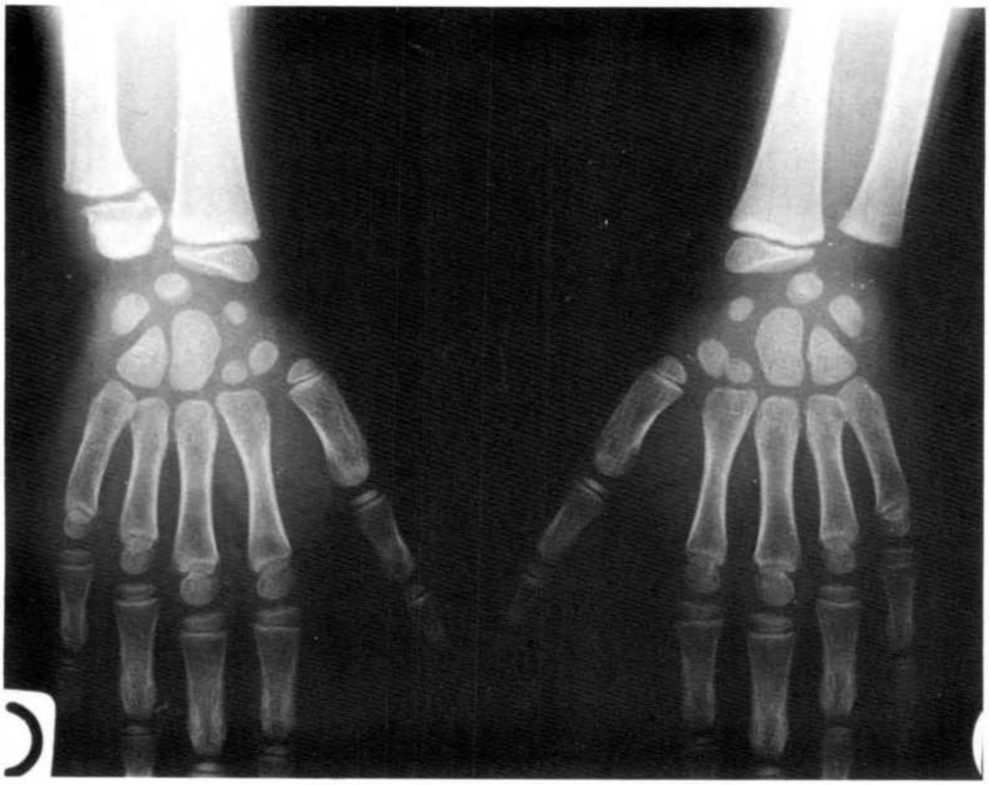

FIG. 1.
Enlarged distal epiphysis of the ulna on the right side; irregular metaphyseal line; shortened ulnar diaphysis. There is no distal ulnar epiphysis on the left side.

The left distal ulnar epiphysis had not appeared and the bone age on both hands was about 6½ years. There was no abnormality of the carpal bones and the remaining skeleton was normal. The diagnosis of dysplasia epiphysealis hemimelica can be established by the presence of this isolated epiphysomegaly.

DISCUSSION

This rare epiphyseal dysplasia was described and recognised as a definite entity by Trevor (1950), who collected 10 cases. The primary defect lies in the epiphyses and the characteristic epiphyseal abnormalities are confined to one side of the affected, usually the lower, limb. Radiological appearances are characteristic. One side only of the epiphysis is involved, except in the case of the smaller tarsal bones. Commonly a number of separate centres of ossification are seen, irregular in shape and size and discrete from the main epiphysis. Swelling increases gradually for the first few years of life, and varus or valgus deformity at a joint may appear. After the age of 6 or 7 years there may be little deterioration.

Radiologically, new centres of ossification may appear and the multiple bony centres increase in size and tend to fuse together into a common mass. Part or all of the outgrowth has been removed in a number of patients, with benefit when there was deformity and pain. Excision of the lesion is indicated when it interferes with function. In our case surgery is not so far indicated.

Case reports of the upper limb are rare and concern carpal bones (Fairbank, 1956; Geschickter & Copeland, 1949; Heiple, 1961; Hensinger et al, 1974; Lamesch, 1983; Saxton & Wilkinson, 1964; Wynne-Davies, 1973) and the radial border of the upper limb (Bigliani et al, 1980; Hensinger et al, 1974; Kettelkamp et al, 1966; Saxton & Wilkinson, 1964). We emphasise the advanced bone age of the abnormal epiphysis (Azouz et al, 1984; Fairbank, 1956; Cruz-Condé et al, 1984; Fevre & Rigault, 1961; Lamesch, 1983; Saxton & Wilkinson, 1964) compared with the epiphysis of the other side. Our example is very unusual because the whole of the epiphysis is affected as in some rare cases (Connor et al, 1983; Fairbank, 1956; Kettelkamp et al, 1966; Trevor, 1950; Wiedemann et al, 1981); this is associated with an equally rare irregular metaphysis (Connor et al, 1983; Fairbank, 1956) and a slightly shortened ulnar diaphysis.

Very few described cases resemble ours, the most similar being that of Buckwalter et al (1978) where the dysplasia involved the distal epiphysis of the ulna in a 3-year-old boy with shortening of both bones of the forearm, bowing of the ulna and abnormal development of the lunate. In a series of patients, Fairbank (1956) described a girl with prominence of the right distal

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ulnar epiphysis at the age of 3 years which gradually resolved. At 12 years old, radiographs of her forearm demonstrated a shortened, bowed ulna with an irregular distal ulnar epiphysis fused to the ulna on the radial side, and an enlarged irregular lunate. However, regression of the prominent epiphysis and early fusion of the epiphyseal plate are not consistent with the common course of dysplasia epiphysealis hemimelica and the abnormalities of this patient's epiphysis could have been secondary to trauma.

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The ultrasonic demonstration of acute multiple gastric ulcers in a child

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Ultrasonography is of proven value in the diagnosis of the acute abdomen in children, notably intussusception and acute appendicitis.

This report describes an unusual case of acute, primary, multiple gastric ulcers in a child. Ultrasonography was used in the establishment of the correct diagnosis and in subsequent follow-up.

CASE REPORT

An 11-year-old boy was admitted to our hospital because of sudden onset of severe, epigastric pain preceded by 2 days of diarrhoea and vomiting On admission, the abdomen was soft, but tender in the upper part. Laboratory tests showed 7100/mm^3 leucocytes and haemoglobin 11.6 g/dl with haematocrit 49.3%. The ultrasonographic examination was performed in the upright position, using a 5 MHz transducer (U-sonic, Model RT 2600, Yokogawa Medical Systems). The stomach was full of gastric juice and there was thickening of the antral gastric wall. After oral administration of 400 ml of water, ultrasonographic examination was repeated and on the transverse scans, two clear ulcerative lesions were shown (Fig. 1A)

Subsequent endoscopic examination confirmed the presence of multiple haemorrhagic ulcers in the antrum Barium examination on the third day after admission also showed multiple, acute ulcers (Fig 2a, b).

The child was treated with cimetidine (800 mg/day) and

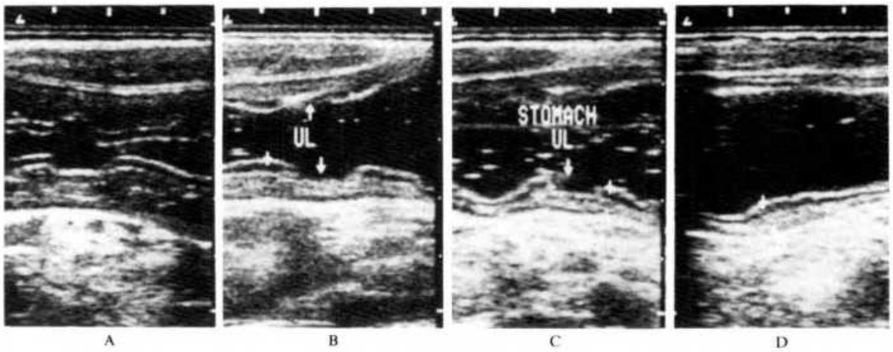

FIG. 1.

(A) On admission, two ulcer craters on the anterior and posterior gastric wall are seen on ultrasound examination. The gastric wall is oedematous and 14 mm thick. (B) On the fourth day after admission, the two ulcer craters are still seen and the gastric wall thickness is 8 mm. (C) On the seventh day, only one ulcer crater is shown and the gastric wall thickness is 7 mm. (D) On the 14th day, there is no ulcer evident and the thickness of the gastric wall has reduced to 6 mm.

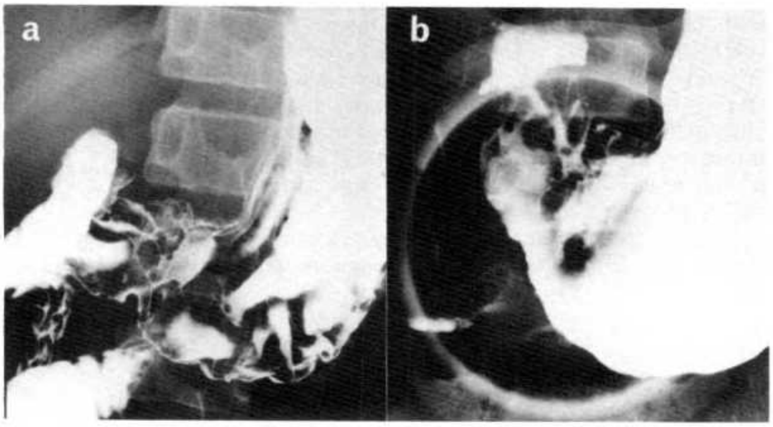

FIG. 2.

(a) On the third day after admission a giant ulcer crater is shown on the posterior gastric wall. (b) Further small ulcers are shown on the anterior wall.

antacids and the clinical course was uneventful. Ultrasonographic examinations were repeated, after oral administration of 400 ml of water, on the fourth, seventh and 14th days after admission. The sequential ultrasonic findings of the ulcers and gastric wall oedema are shown in Fig. 1 (B–D). The upper gastrointestinal series on the 15th day after admission is shown in Fig. 3.

DISCUSSION

Multiple gastric ulcers in children are not common, but peptic ulceration is being diagnosed more commonly, possibly as a result of social change and also because of improved diagnostic procedures, including endoscopy. The main symptoms of gastric

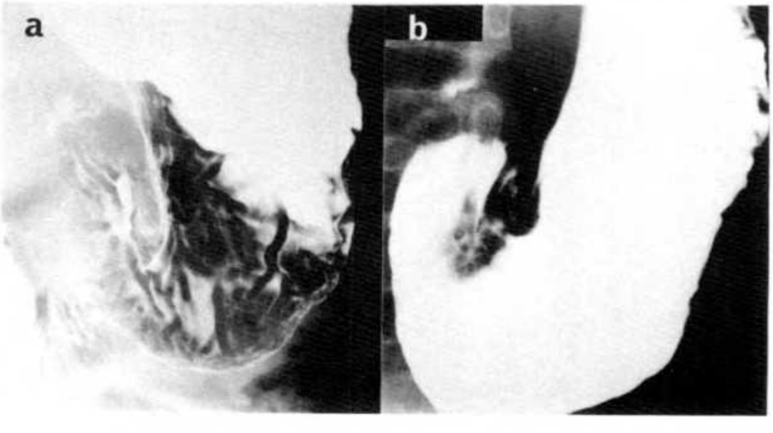

FIG. 3.

(a) On the 15th day, healing of the posterior ulcer is seen. (b) Other ulcer scars are also shown.

ulcers are pain and bleeding, which need to be differentiated from other causes of acute abdomen.

With recent development of both apparatus and diagnostic techniques, ultrasonography has become a primary diagnostic tool in disease within the abdominal cavity, notably the gallbladder, liver and kidney, but in gastric lesions, it has played mainly a supportive role.

The diagnosis of gastric ulcer is still made by X-ray contrast examination or endoscopy. Up to now, a few adult cases of peptic ulcer diagnosed by ultrasound have been reported (Madrazo et al, 1981; Nyberg & Laing, 1983; Parulekar & Lubert, 1983; Catalano & Troianiello, 1984) but these were duodenal ulcers which had perforated or formed fluid collections. A single adult case of gastric ulcer diagnosed by ultrasound has been reported as showing a collection of dense echoes with a strong acoustic shadow in the antrum in the acute phase (Rosenberg et al, 1980).

In our child, ultrasonic examination revealed gastric wall oedema as well as ulcer craters and their subsequent changes. This successful demonstration probably results from the ulcerative lesions being severe, multiple and in the acute phase, and that the ultrasound examination was performed using a 5 MHz transducer in the upright position with good distension of the gastric wall following oral administration of 400 ml of water.

The symptoms subsided gradually with treatment and the gastric ulcers, on ultrasonic examination, were seen to heal almost completely. His clinical course was uneventful.

Ultrasound is easy and convenient to use with no significant patient discomfort and we believe it should be used more frequently as a general screening procedure for children with upper abdominal complaints as well as blood count and radiography of abdomen and chest.

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Case of the month

The case of the forgetful gardener

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(*Received May 1986*)

A 46-year-old gardener was admitted for the investigation of unsteadiness of gait and increasingly poor memory. He gave an 18-month history of poor co-ordination and increasing weakness of the right arm and leg. He was known to have been epileptic for over 20 years, but his fits had increased in frequency recently, despite appropriate medication.

On examination he was found to be apyrexial and normotensive. There was a pyramidally distributed weakness of his right arm and leg, and bilateral cerebellar intention tremor, more marked on the right than on the left. His gait was ataxic. He was temporally disorientated and had impaired short- and long-term memory.

Biochemical, haematological and serological investigations were all normal. The ESR was 15 mm/h (Westergren). By lumbar puncture, his cerebrospinal fluid was found to be under normal pressure with 16 lymphocytes/mm^3, and a protein of 950 mg/l, with a negative VDRL. Visual evoked responses showed significantly delayed latencies bilaterally.

The chest radiograph was normal. Cerebral scintigraphy (Fig. 1), was abnormal and computed tomography (CT) was performed (Fig. 2).

What diagnoses would you have considered at this stage?

A trial course of ACTH produced no benefit and he slowly deteriorated. He died a year later from an intercurrent chest infection.

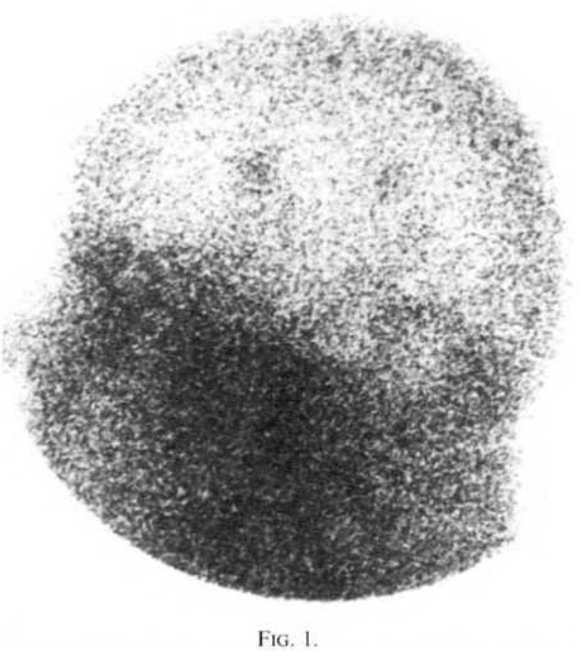

FIG. 1.

Lateral cerebral scintigram with DTPA, showing two areas of increased photon emission over the temporo-parietal region.

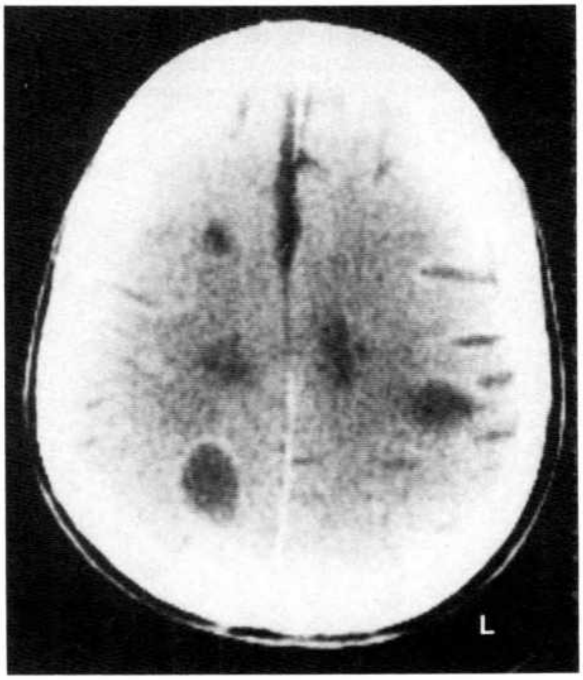

FIG. 2.

Post-contrast CT scan at the upper limit of the lateral ventricles, showing three well defined hypodense lesions. Rim enhancement can be seen around the lesion in the right parieto-occipital lobe.

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The CT scans show several discrete enhancing hypodense areas in the white matter. The differential diagnosis of such lesions includes multiple cerebral infarcts, metastases and abscesses. All of these lesions might also be expected to show areas of increased activity on a cerebral DTPA scan, as they alter the "blood–brain barrier".

Infarcts are usually limited to one vascular territory, and involve both white and grey matter. Abscesses are usually associated with fever and leucocytosis. There was no evidence of any extracerebral metastatic deposit nor of any primary neoplastic source.

A fourth diagnosis should be considered when these appearances are seen: multiple areas of acute demyelinisation.

At post-mortem examination, the brain showed numerous macroscopic areas of pinkish-yellow discoloration, predominantly in the white matter of the midbrain, pons and medulla, as well as the cerebral hemispheres (Fig. 3). Microscopy showed active, ongoing demyelination associated with intense inflammation. There was relative axonal preservation. This was considered to be due to acute multiple sclerosis of the Marburg type.

Multiple sclerosis is the second commonest neurological disease of young adults in this country, making knowledge of its radiological features important. It may be seen in its classical, familiar form, or acute Marburg-type disease. In Marburg type, which may be accompanied by a mild fever, the demyelinating process is fulminant and the patient often deteriorates rapidly. The lesions show extensive myelin destruction and oedema (Allen, 1984).

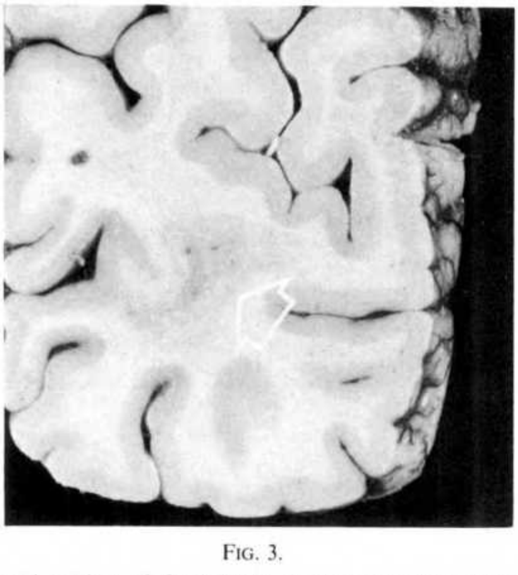

FIG. 3.

Coronal section of fixed brain through the right parieto-occipital lobe illustrating a typical lesion within the white matter (arrow).

In multiple sclerosis exacerbations, myelin is lost, increasing the overall water concentration of the focus of affected white matter, rendering it hypodense on CT scans. Enhancement with contrast medium is suggestive of disease activity and as each lesion remits, it loses its enhancing capability. Enhancement can diminish on treatment with steroids without necessarily any simultaneous clinical improvement. Chronic lesions may remain hypodense or return to isodensity relative to the adjacent brain substance (Weinstein et al, 1978). Cerebral atrophy and generalised ventricular enlargement may be seen. The lesions visualised by CT tend to be cerebral. At necropsy 74% of lesions are in the white matter, with 40% in the periventricular areas or elsewhere in the white matter of the midbrain or cerebellum, and 10% in the grey matter.

Vinuela et al (1982) have reported a technique of high-volume delayed scanning using a bolus injection of contrast medium, containing 40 g of iodine, followed by a rapid intravenous infusion of a further 42 g of iodine, with scanning beginning 1 h after the rapid drip infusion. This technique substantially increases the number of multiple sclerosis lesions shown when compared with conventional enhancement techniques.

Nevertheless, lesions visualised by CT may correspond only poorly with the clinical neurological signs, suggesting that there may be some residual neural conduction through lesions identified by CT, and also that further clinically significant lesions are not being identified.

Magnetic resonance imaging (MRI) can better demonstrate the number, position and size of lesions, particularly if they are small or in the brain stem (Young et al, 1981). Such lesions are typified by slow relaxation times, relative to normal white matter. However, as Ebers et al (1984) state, it remains doubtful whether MRI is as accurate as CT in assessing the integrity of the blood–brain barrier, which is a useful indicator of disease activity.

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Short communications

The role of delayed computed tomographic scanning using high doses of contrast material in detecting cerebral demyelination in patients with multiple sclerosis in relapse and remission

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Multiple sclerosis (MS) is a relapsing and remitting condition leading to periventricular plaques of demyelination During the acute stages of plaque formation, the blood–brain barrier may break down but in chronic plaques of demyelination the barrier is characteristically intact (Jann Brown, 1978). Three studies have shown that the use of higher than conventional doses of ionic contrast medium, with or without delayed computed tomographic scanning, demonstrates increased numbers of plaques of cerebral demyelination in patients with MS (Sears et al, 1982; Vinuela et al, 1982; Spiegel et al, 1985). The first two studies were carried out on MS patients in relapse alone, while the third was performed on a heterogeneous group of MS patients, some in relapse and some in remission.

In this study, computed tomographic (CT) brain scans were carried out on two groups of MS patients, one in remission and one in relapse Scans were enhanced both conventionally and using high volumes of non-ionic contrast medium with delayed scanning (HVC technique). The number of additional plaques shown by the HVC technique was compared for the two groups of MS patients.

METHODS

Computed tomographic brain scans were carried out on 10 patients with MS in clinical remission and on nine patients 2–6 weeks following clinical relapse All patients had clinically definite MS or laboratory-supported definite MS according to the classification of Poser et al (1983). Patient details are shown in Tables I and II. Informed consent was obtained from all subjects before CT scanning and the research project was approved by the Ethics Committee of the Royal Postgraduate Medical School.

The CT scans were performed on a Siemens Somatom 2 scanner using 8 mm contiguous slices An unenhanced scan was performed and then 100 ml of iohexol 300 (Omnipaque 300, Nycomed UK Ltd) was administered as an intravenous bolus and the scan repeated Following this an infusion of 150 ml of iohexol 300 was administered intravenously over a period of 45 min, and a final scan was then performed after 60 min. No significant adverse reactions to the contrast medium were observed.

RESULTS

The numbers of plaques of cerebral demyelination seen on the CT brain scans of the remission and relapse groups are detailed in Tables I and II, respectively. The HVC technique demonstrated only one additional cerebral plaque in the group of 10 patients in remission, and obscured a cerebral plaque evident on the unenhanced CT brain scan of one of these patients. The HVC technique demonstrated additional plaques in three out of the nine MS patients studied after relapse and emphasised a plaque evident on the unenhanced CT brain scan of a fourth patient

The unenhanced, conventionally enhanced, and HVC CT brain scans of a patient with MS in relapse are shown in Fig. 1. A periventricular lucency is evident on the unenhanced scan (Fig 1A). Following administration of 250 ml of non-ionic contrast medium the 60 min scan (Fig. 1C) shows an obvious enhancing right frontal plaque not present on the first post-contrast scan (Fig. 1B).

DISCUSSION

The plaques demonstrated in CT brain scans of patients with MS have been shown to correlate with plaques found at autopsy (Lane et al, 1976; Haughton et al, 1979). The uptake of intravenous contrast medium by cerebral lesions on CT scans has been shown to be associated with the presence of blood–brain barrier disruption (Gado et al, 1975) and the presence of such enhancing lesions in MS patients in relapse has been well documented (Harding et al, 1978, Sears et al, 1978). Morariu et al (1980) first suggested that delaying CT scanning after intravenous contrast-medium administration might increase the yield of enhancing cerebral lesions in MS. Since then three series have been published showing a significantly increased detection of plaques of demyelination in MS patients using a high volume of intravenous contrast medium with or without delayed scanning (Sears et al, 1982, Vinuela et al, 1982; Spiegel et al, 1985).

Our study has shown a negligible benefit from using the HVC technique in MS patients in remission. Plaque detection was the same in the enhanced and non-enhanced studies (Table I). This finding is in line with electron-microscopic studies on chronic MS plaques which show an intact blood–brain barrier (Jann Brown, 1978). An increased number of cerebral lesions was detected in the group of MS patients in relapse using the HVC technique compared with standard contrast enhancement. This difference failed to reach a 5% level of significance, however, when a Student's paired *t*-test was applied, and additional lesions were demonstrated in only three out of the nine MS patients studied during relapse using the HVC approach.

In conclusion, the HVC approach appears to offer no additional advantage in demonstrating plaques of demyelination in MS patients in remission. Those MS patients in relapse who had normal unenhanced CT brain scans also failed to show any additional lesions following high-volume

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TABLE I

REMISSION MS PATIENT DETAILS AND CT SCAN FINDINGS

Sex	Age (years)	Diagnosis of MS	CT brain scan		
			Unenhanced	Enhanced	HVC
F	50	CD	Atrophy	2 plaques	No plaques
F	27	CD	Atrophy, 6 plaques	No change	No change
F	52	LSD	Central atrophy	No change	1 plaque
M	51	CD	Normal	No change	No change
F	37	LSD	Normal	No change	No change
F	61	CD	Atrophy	No change	No change
F	41	CD	Normal	No change	No change
F	54	CD	Atrophy, 8 plaques	No change	No change
F	47	LSD	Normal	No change	No change
F	39	CD	1 plaque	Plaque less clear	Plaque less clear
			15 plaques total	17 plaques total	16 plaques total

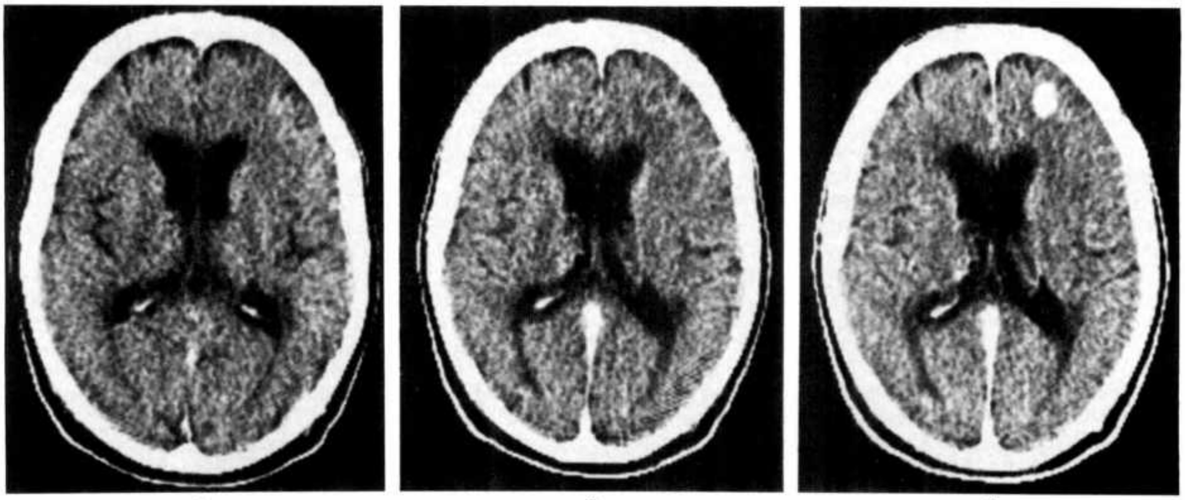
CD = clinically definite, LSD = laboratory-supported definite.

TABLE II

RELAPSE MS PATIENT DETAILS AND CT SCAN FINDINGS

Sex	Age (years)	Diagnosis of MS	Duration of relapse (weeks)	CT brain scan		
				Unenhanced	Enhanced	HVC
M	41	LSD	6	1 plaque	1 plaque	2 plaques
F	20	CD	2	1 plaque	Plaque clearer	Plaque much clearer
F	69	CD	2	Central atrophy	1 plaque	3 plaques
F	37	LSD	6	Normal	No change	No change
F	55	CD	3	Normal	No change	No change
F	28	CD	2	Normal	No change	No change
F	23	LSD	2	Normal	No change	No change
F	18	CSD	1	1 plaque	No change	No change
F	27	CSD	4	3 plaques	No change	7 plaques
				6 plaques total	7 plaques total	13 plaques total

CD = clinically definite, LSD = laboratory-supported definite.



A B C

FIG. 1.

(A) Unenhanced, (B) conventionally enhanced, and (C) HVC CT brain scans of a patient with MS in relapse.

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contrast-medium administration. Of the four MS patients in relapse who had plaques evident on their unenhanced CT brain scans, two had additional lesions evident on the HVC scan and a third had a lesion emphasised. Our results suggest that in practice the HVC technique will give extra information only in MS patients in relapse with plaques already evident on their unenhanced CT scans.

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Low-dose total-body irradiation in the management of refractory rheumatoid arthritis

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The use of radiotherapy in the treatment of arthritides has a history almost as long as to Roentgen's discovery of X rays in 1895; indeed, X-ray treatment was the prime management of ankylosing spondylitis for over 30 years until the evidence of late risk of induction of malignancy led to premature near-abandonment of its use. The risks are now well quantified (Smith et al, 1977; Smith & Doll, 1982) and the therapeutic value of irradiation is being reassessed in the light of the undoubted toxicity of alternative forms of treatment (*e.g* Smythe, 1979; Calman & Berry, 1980, Bamji et al, 1982). Rheumatoid arthritis is a chronic systemic disease which is characterised by the presence of aetiological factors which set into motion humoral immune mechanisms and cell-mediated immunity (Anonymous, 1982). The rationale for using radiotherapy in the treatment of refractory rheumatoid arthritis is its capability for immunosuppression (Schurman et al, 1981, Weigensberg et al, 1984) and immunological modification (Tanay et al, 1984; Field et al, 1984) Total lymphoid irradiation, developed for the treatment of Hodgkin's disease, has been used for the treatment of patients with severe rheumatoid arthritis with some success (Calin, 1985), but is technically very demanding in these extremely handicapped patients. Low-dose total-body irradiation (TBI) is also immunosuppressive and has been little used in the treatment of non-malignant conditions such as polymyositis (Engel et al, 1981; Hubbard et al, 1982) and rheumatoid arthritis (Urowitz & Rider, 1985). We report here a small series of patients treated with TBI for refractory and progressive rheumatoid arthritis.

METHODS

Four patients received a midline absorbed dose of 150 cGy (rad) in either 10 or 15 daily fractions over a period of 16–23 days with 8 MV X rays from a linear accelerator. The dose rate at the midline was 12–14 cGy/min. The patients were either seated in or knelt on a chair in a semi-fetal position. Irradiation was by means of parallel opposed lateral fields at a focus–skin distance (FSD) of 345 cm, giving a maximum field size at the patient of 103.5 cm. The patients were rotated through 180° for alternate treatments. For the four patients, the separation, measured across the shoulders, was between 36 cm and 46 cm, giving a midline central axis depth dose of between 63% and 54%. No build-up was used and the dose maxima along the beam central axis, which occur at 2 cm below the skin, were between 109% and 116% of the midline dose. For the head, the midline doses are of course considerably higher because of the smaller separation. Head separations were not recorded but, using a reasonable average figure of 15 cm and allowing for the increase in FSD to the head, midline doses were calculated to be between 135% and 150% of the midline dose at shoulder level. No pre-medication was given and the treatment was tolerated without symptomatic side-effects. One patient who had previously been treated with chlorambucil and azathioprine (stopped 3 months before TBI) developed neutropenia (0.77×10^9) and thrombocytopenia (7×10^9) which required hospitalisation, platelet transfusion and reverse-barrier nursing, but recovered without further intervention by approximately 5 weeks after her TBI. None of the other patients required haematological support. All patients have now been followed up for a minimum of 4 years, or until relapse, their clinical response to treatment has been assessed by measuring total active joint count (tenderness and/or swelling), erythrocyte sedimentation rate and peripheral blood count (haemoglobin, lymphocyte count, differential and platelet count).

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PATIENTS

E. R. is a male with erosive nodular rheumatoid arthritis of long duration (since 1968) who was 51 years old at the time of his TBI in 1981. He had been treated previously with gold, prednisolone and dapsone. There was dramatic initial improvement which was not maintained for more than 3 months and he was started on long-term steroid maintenance. By 2 years after TBI his disease remained less active than before irradiation but he had dreadful joint damage. In August 1985 his disease was again active and in May 1986 he was started on intermittent methotrexate chemotherapy in an attempt to achieve a further remission.

C. B. was a female with a history of severe seropositive rheumatoid arthritis since 1975, who was 46 at the time of her TBI in 1982. She had previously been treated with prednisolone, gold, penicillamine, non-steroidal anti-inflammatory drugs, chlorambucil (2 weeks only) and azathioprine which was stopped 3 months before her TBI. She was the only patient who required hospitalisation during her haematological nadir (see above) but had a dramatic symptomatic and objective improvement. She had one bout of severe menorrhagia and remained mildly anaemic, suffered from depression, but showed no evidence of recurrent activity of her disease on only prednisolone and non-steroidal anti-inflammatory drugs. She suffered a fractured femur due to trauma in October 1984 and tragically died in a fire caused by a cigarette which she was smoking in bed in December 1984, but had no evidence of progression of her rheumatoid arthritis until her death.

Y. C. is a female whose aggressive seropositive rheumatoid arthritis was first diagnosed in 1978. She was only 30 years old when she received her TBI in 1982, but had previously been treated without success with penicillamine, sodium aurothiomalate, prednisolone, dapsone and non-steroidal anti-inflammatory drugs. She had dramatic and almost immediate relief of her symptoms, and objective improvement which lasted for 3–4 months, but since then has made continuous progress even though she has had to undergo orthopaedic intervention to improve function in the right wrist.

A. D. is a female who was 58 years old at the time when her severe rheumatoid arthritis of long duration was treated by TBI in 1984. She had been treated previously with penicillamine, gold and prednisolone and although her condition remained stable and her disease less active for a period of 6 months, she then showed unmistakable progression.

DISCUSSION

Low-dose TBI has been dismissed as having a small role to play in the management of severe rheumatoid arthritis (Calin, 1985) and we report this small series of patients only to demonstrate that this non-upsetting treatment is capable of inducing remissions which are durable in some patients. The benefit obtained is undoubtedly due to the depression in peripheral lymphocyte count, although radiation also has effects on lymphocyte function (Anderson et al, 1977; Kotzin et al, 1984). Total lymphoid irradiation (TLI), used for many years to treat Hodgkin's disease, is profoundly immunosuppressive and it is this which probably underlies its demonstrated effectiveness in the treatment of severe rheumatoid arthritis (Calin, 1985). Total-body irradiation offers advantages over TLI in the ease of radiotherapy planning and patient positioning—not a negligible consideration in these often severely crippled patients. It is largely free of acute side-effects and does not require hospitalisation. The long-term risk of leukaemogenesis or carcinogenesis is not yet known but prior experience of the treatment of patients with ankylosing spondylitis and the use of TBI in the treatment of non-Hodgkin's lymphoma suggests that it will be acceptably low. Cytotoxic drugs which are immunosuppressive are also effective in the treatment of rheumatoid arthritis, but at least some (such as the alkylating agents) are themselves unacceptably leukaemogenic or carcinogenic. So far, azathioprine appears to lack this late side-effect (Schwartz, 1984). However, the combination of prior radiotherapy and cytotoxic chemotherapy appears to result in a major excess of secondary malignancies (Canellos et al, 1975). At the moment, we do not know the relative benefits and risks of radiation and drugs used as immunomodulators in the long-term management of rheumatoid arthritis. Proper double-blind trials have established the value of TLI in the treatment of severe rheumatoid arthritis (Calin, 1985); we feel that it is time for similar studies, with true informed patient consent, to be carried out using low-dose total-body irradiation.

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We would like to thank Dr M. Corbett, Consultant Rheumatologist, for referring the patients, for subsequent critical evaluation of their clinical progress, and for helpful advice. Treatment planning and the calculation of dose distribution were carried out by Dr Beate Planskoy and her team in the Medical Physics Unit, and its delivery organised by Miss Pauline Curtis, Deputy Superintendent Radiographer (Planning) and our devoted team of radiographers.

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

What minimum number of fractions is required with high dose-rate remote afterloading?

THE EDITOR—SIR,

In his excellent article on the use of the linear quadratic (LQ) model for protracted radiotherapy, Dale (1985), in one of his examples, used this model to show that fractionated high dose-rate treatments would be equivalent to the conventional low dose-rate regimens they replace only if about 17 fractions could be given. This is a vitally important conclusion owing to the rapidly expanding use of high dose-rate remote afterloading, especially for the treatment of cancer of the cervix, where most radiotherapists would approach the use of 17 applications of the intracavitary hardware on outpatients with considerable apprehension.

Fortunately, as shown below, a more rigorous application of the LQ model to this question demonstrates that considerably fewer than 17 fractions are needed for equivalence.

In Dale's analysis, it was assumed that the rate of repair of sublethal cellular damage, represented by the repair coefficient $\mu\ \mathrm{h}^{-1}$, was the same for early-reacting tissues (and tumours) as for late-reacting tissues. However, this is clearly an over-simplification introduced to equate high and low dose-rate regimens with the LQ model, since elsewhere in his paper, he states that better estimates for the values of μ are $1.4\ \mathrm{h}^{-1}$ for early-reacting tissues (and tumours*) and $0.32\ \mathrm{h}^{-1}$ for late-reacting tissues, instead of the "compromise" value of $0.46\ \mathrm{h}^{-1}$ assumed. It will now be shown that this simplification was unnecessary.

Assume that the values of μ and α/β for tumours and late-reacting tissues are μ_t, $(\alpha/\beta)_t$, and μ_l, $(\alpha/\beta)_l$, respectively. Then, for the high dose-rate fractionated treatments, the extrapolated response dose (ERD) corresponding to local control of the tumour in N_t fractions each of dose d is:

$$(\mathrm{ERD})_t = N_t d\left(1+\frac{d}{(\alpha/\beta)_t}\right)$$

and, for late-reacting tissues the ERD corresponding to "tolerance" in N_l fractions of dose d is:

$$(\mathrm{ERD})_l = N_l d\left(1+\frac{d}{(\alpha/\beta)_l}\right)$$

Then the therapeutic ratio ($\mathrm{TR}_{\mathrm{HDR}}$) for these high dose-rate (HDR) treatments, which is given by the ratio of the tolerance to tumoricidal doses, is:

$$\mathrm{TR}_{\mathrm{HDR}} = \frac{N_l d}{N_t d} = \left[\left(1+\frac{d}{(\alpha/\beta)_t}\right)\bigg/\left(1+\frac{d}{(\alpha/\beta)_l}\right)\right]\cdot\frac{(\mathrm{ERD})_l}{(\mathrm{ERD})_t}$$

For the conventional low dose-rate (LDR) treatments, the ERD for tumours in time T_t at dose rate R is approximately (Dale, 1985):

$$(\mathrm{ERD})_t = T_t R\left(1+\frac{2R}{\mu_t(\alpha/\beta)_t}\right)$$

where T_t represents the overall sum of the treatment times for all applications. This equation is a good approximation when T_t approaches 100 h, which is typical of conventional LDR techniques. For late-reacting tissues, in time T_l and at dose rate R:

$$(\mathrm{ERD})_l = T_l R\left(1+\frac{2R}{\mu_l(\alpha/\beta)_l}\right)$$

and the therapeutic ratio ($\mathrm{TR}_{\mathrm{LDR}}$) for these LDR treatments is:

$$\mathrm{TR}_{\mathrm{LDR}} = \frac{T_l R}{T_t R} = \left[\left(1+\frac{2R}{\mu_t(\alpha/\beta)_t}\right)\bigg/\left(1+\frac{2R}{\mu_l(\alpha/\beta)_l}\right)\right]\frac{(\mathrm{ERD})_l}{(\mathrm{ERD})_t}$$

The relative efficacy of HDR compared with LDR treatments is determined by the TRs, *i.e.* HDR is equivalent to or better than LDR if $\mathrm{TR}_{\mathrm{HDR}} \geqslant \mathrm{TR}_{\mathrm{LDR}}$,

$$\text{or}\ \left(1+\frac{d}{(\alpha/\beta)_t}\right)\bigg/\left(1+\frac{d}{(\alpha/\beta)_l}\right) \geqslant \left(1+\frac{2R}{\mu_t(\alpha/\beta)_t}\right)\bigg/\left(1+\frac{2R}{\mu_l(\alpha/\beta)_h}\right) \quad (1)$$

Also, in order to maintain the same level of effect on late-reacting tissues, a second condition must be met, namely:

$$[(\mathrm{ERD})_l]_{\mathrm{HDR}} = [(\mathrm{ERD})_l]_{\mathrm{LDR}} \quad (2)$$

It should be noted that, since the LQ model does not account for the effect of overall treatment time, it has been assumed that the total treatment times for the intracavitary plus external-beam regimes are the same for the HDR and LDR courses. It has also been assumed that the external-beam treatments used to supplement intracavitary irradiations are the same for the HDR and LDR techniques. Hence, the effect of external-beam doses upon the therapeutic ratios is the same.

In order to determine the minimum number of fractions required for equivalence, specific values for the parameters need to be inserted into Equations (1) and (2) above. Two examples of the solution to the cervical cancer problem (Example B) in Dale's paper are given below.

Example 1: same value of μ

In Dale's Example (B), the minimum number of fractions N required to replace a conventional course of cervical cancer intracavitary treatments with overall time 72 h at $0.833\ \mathrm{Gy\ h}^{-1}$ is determined assuming $\mu_t = \mu_l = 0.46\ \mathrm{h}^{-1}$, $(\alpha/\beta)_t = 10$ Gy, $(\alpha/\beta)_l = 2.5$ Gy. Inserting these values into Equations (1) and (2) gives the equivalent HDR regimen as 16.6 fractions of 3.61 Gy.

It should be noted that, for simplicity, the ERD calculations for the LDR treatments above were made using the approximate form of the ERD formula (Equation E in Dale's paper), which is appropriate for overall treatment times of about 100 h or more. In the above example, this time was only 72 h. Use of the more accurate ERD formula (Equation D in Dale's paper) makes only a small difference to the answer to this example, viz. the equivalent HDR regimen is *17.0 fractions of 3.53 Gy*. This is the same answer as was obtained by Dale.

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*Although Dale (1985) does not specifically state that the values of μ and α/β for tumours are similar to those for early-reacting tissues, he uses early-reacting tissue damage values of μ and $\alpha 7\beta$ to relate to tumour response. Similarly, Thames et al (1984) showed that μ values for early-reacting tissues are small compared with those for late-reacting tissues and then used these differences to demonstrate that fractionation, especially hyperfractionation, leads to a therapeutic advantage when comparing tumour-cell destruction to late tissue damage. They thus imply that values of μ for tumours can be represented by those for early-reacting tissues.

Example 2: different values of μ

Solving the same problem with the same parameters as above except that $\mu_t = 1.4\,h^{-1}$, and $\mu_l = 0.32\,h^{-1}$, and using the accurate form of the ERD equation for low dose rate, yields an equivalent HDR regimen of *2.36 fractions of 12.6 Gy*.

Delivering more than this minimum number of fractions increases the efficacy of HDR treatments. This is illustrated in Table I, which shows how the ratio of the high and low dose-rate therapeutic ratios increases as the number of HDR treatments increases. It would appear that the relative efficacy of the HDR treatments continues to increase as the number of fractions increases. However, the LQ model ignores the effects of overall treatment time. Unless multiple daily fractions of the HDR treatments are given, the overall time needs to be increased after more than about 30 fractions. Presumably, tumour cell proliferation might then begin to be a problem, and the ratio of TRs will fall below the "ideal" values shown.

It is also important to realise that Table I shows the ratio of TRs only for the intracavitary parts of the treatment of these patients. The external-beam components will tend to "dilute" the apparent advantage of the HDR treatments for more than three fractions and the values shown in Table I represent the upper limits for this improved ratio of TRs.

Thus, by using the values of μ and α/β suggested by Dale for early- and late-reacting tissues, the LQ model predicts that a typical LDR regimen for the treatment of cervical cancer can be replaced by a fractionated HDR technique provided the number of fractions is greater than about three. Moreover, if more than this minimum number of fractions is given, then the HDR technique will result in an improved therapeutic ratio when compared with the conventional LDR regimen that it replaces. It should be realised, however, that the actual value determined for the minimum number of HDR fractions required for equivalence depends upon the values of μ and α/β used in the calculations, and also upon the validity of the LQ model for brachytherapy. All of these are relatively "unknown". This letter is intended simply to demonstrate that it is likely that relatively few HDR fractions might well provide this equivalence to the conventional LDR techniques they replace.

Yours, etc.,
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(*Author's reply*)

THE EDITOR—SIR,

Dr Orton has presented a useful mathematical analysis which I agree with insofar as it represents an interesting way of finding the theoretical maximum dose/fraction which can be used when switching from a protracted LDR treatment to a fractionated HDR regimen. However, the assertion that his particular numerical example (Example 2 of his letter) represents a "more rigorous application of the LQ model" is misleading, since his predictions are only valid for tissues which can be described in terms of the parameter values he has chosen to use and, on this point, he has misquoted the use of the damage repair constants in my own paper (Dale, 1985).

Firstly, I did not use early-reacting μ values to relate to tumour response, as stated in Dr Orton's footnote. Neither did my article give worked examples which related specifically to tumour effects. While it is true to say that a substantial amount of evidence suggests that α/β values for early-responding reactions and tumour effects are *broadly* similar, I deliberately refrained from implying that the respective μ values associated with these two effects might similarly correspond.

Denekamp (1986) has indicated that some preliminary studies show that repair rates in some tumours are indeed high. However, based on experimental findings with other tissues, it is reasonable to expect that, as more recovery values become known, they will be found to cover a fairly broad band. Thames et al (1984) found early-reacting μ values to be in the range 0.77–2.31 h^{-1}. Therefore, even assuming that tumour and early-reacting tissue recovery constants do cover a similar spread, Dr Orton's selection of a middle value ($1.4\,h^{-1}$) to represent tumour response is itself an oversimplification.

Secondly, I did not state that $\mu = 0.32\,h^{-1}$ was a better estimate than $\mu = 0.46\,h^{-1}$ for late-reacting tissues. In my article, the recovery constant of $0.32\,h^{-1}$ was derived from Mitchell's (1960) data, which were clearly stated to relate to the minimum dose required for the healing of small skin tumours. This suggests that the μ value calculated from these data is applicable to a tumour response rather than late-reacting effects. However, as Mitchell's tabulations were based on articles originally published in 1936, I again refrained from being too dogmatic on this point, and used the exercise to demonstrate how, in principle, μ values could be obtained from clinical data.

The more representative μ value to use for late-reacting tissues is $\mu = 0.46\,h^{-1}$, as used in my article, since this has recent experimental foundation (Thames, 1984). When used in Dr Orton's Equation (1), in conjunction with his assumed tumour recovery constant of $1.4\,h^{-1}$, the predicted value of d_{max} becomes 6.6 Gy, and the minimum fraction number becomes approximately six. This latter value contrasts with the value of about two obtained by Dr Orton when using the equation with a late-reacting μ value of $0.32\,h^{-1}$. The values given in his Table I are also unrepresentative, for the same reason.

The main point which emerges is that great care is required when using the model to make clinical predictions, particularly when the parameter values involved fall within a wide range of possibilities. It is prudent to use the LQ model to analyse the worst possible case as well as the best possible case.

Additionally, it must be remembered that it is probable that the LQ model begins to break down when large values of dose/fraction are involved (*e.g.* Gilbert et al, 1980). The exact threshold of unreliability is difficult to define, but Thames

1987, *The British Journal of Radiology*, 60, 302–303

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TABLE I

THE RELATIVE EFFICACY (RATIO OF THERAPEUTIC RATIOS) OF HDR COMPARED WITH LDR REGIMENS FOR THE INTRACAVITARY COMPONENT OF CERVICAL CANCER TREATMENTS ONLY, AS A FUNCTION OF THE NUMBER OF HDR FRACTIONS, KEEPING LATE-TISSUE REACTIONS CONSTANT

No. of fractions	Dose/fraction (Gy)	Total dose (Gy)	TR_{HDR}*/TR_{LDR}
1	20.00	20.00	0.89
2	13.80	27.60	0.98
3	11.06	33.18	1.04
5	8.32	41.60	1.13
10	5.57	55.70	1.29
15	4.37	65.55	1.40
20	3.66	73.20	1.48
30	2.82	84.60	1.61

* The accurate form of the ERD formula (Equation D in Dale's paper) has been used.

(1985) has shown that, for some cell lines, the LQ approximation may not be strictly valid for doses/fraction well in excess of 4 Gy. Therefore a calculated value as high as 12.6 Gy, as in Dr Orton's example, must be regarded with an additional degree of scepticism.

On the wider issue of high dose-rate afterloading, it is certainly true that many centres use relatively small fraction numbers without any apparent deterioration of treatment quality. That this is so may well be more directly related to the accurate geometrical positioning of sources and spacers which is possible with such techniques, thereby limiting the dose to sensitive organs, rather than to purely radiobiological reasons. Indeed, a complete theoretical analysis of the likely changes in therapeutic ratio is only possible if full account is taken of the fact that normal-tissue and tumour doses in brachytherapy are often very different, both from each other and from the nominal dose which is used to describe a complete treatment.

Yours, etc.,
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Radiation response of multicellular spheroids initiated from five human melanoma xenograft lines

THE EDITOR—SIR,

In their recent report on the radiation response of human melanoma lines grown *in vitro* as multicellular spheroids, Rofstad et al (1986) commented on discrepancies between the doses of radiation at which a proportion of spheroids were "cured" (those that did regrow, arising from "spheroid-regenerating units", SRUs) and the doses that would be predicted to be curative on the basis of survival curves for clonogenic cells disaggregated from irradiated spheroids. They noted that the data were consistent with a lower number of SRUs than clonogenic cells per spheroid, although they did not pursue this observation quantitatively We have suggested previously that tumour spheroids may be particularly useful in unravelling the relationships between tumour-regenerating units and clonogenic cells, with respect to parameters such as relative number and sensitivity to radiation (Moore & Hendry, 1984) Accordingly, we have further analysed the data of Rofstad et al, using (i) a multitarget-type equation to measure parameters of clonogenic survival for cells disaggregated from spheroids that had been irradiated 18 h previously (measuring the mean lethal dose, D_0, of the final part of the dose–response curves, and E, the single-unit extrapolation number), and (ii) a double negative log equation (Gilbert, 1974) to determine for the SRUs their D_0 and also the extrapolation number of the *spheroid* survival curve, NE which is the product of the number (N) of SRUs in the spheroid and the extrapolation number (E) of the individual SRUs. The assumptions involved in the procedure and the interpretations of its outcome have been discussed recently by Hendry and Thames (1986).

Results are shown in Table I. Of particular interest was that in these small, well oxygenated spheroids (Rofstad et al, 1986), all or almost all of the variation in the response to radiation of the whole spheroids (the steepness of the curve of spheroid "cure" versus dose) can be accounted for by *inherent* Poisson variation in the response of SRUs that have the same D_0 as the clonogenic cells in the spheroid Only for line GE were the D_0s significantly different (that from the cure curve being steeper; $p = 0.045$). Also, a common D_0 (0.93 ± 0.03 Gy) could be fitted to all eight sets of data, the total variation being not significantly different from that for the independent fits ($p = 0.118$)

In a previous analysis of the response of larger spheroids containing hypoxic fractions of cells, the derived D_0 for SRUs was larger than that measured experimentally for clonogenic cells after high doses of radiation, probably because of the additional heterogeneity of response introduced by the different hypoxic fractions among spheroids (Hendry & Moore, 1984; Moore & Hendry, 1984).

Calculation of the number of SRUs per spheroid, by

TABLE I

CELL-SURVIVAL PARAMETERS AFTER IRRADIATION OF SPHEROIDS OF FOUR HUMAN MELANOMA LINES

Spheroid line	VN	EE	MF	GE
(1) Spheroid dimensions				
Diameter ±1 SE	100±5	100±5	100±5	100±5
Histologically intact cells per spheroid	400–500	400–500	400–500	400–500
(2) Cell-survival parameters for clonogenic cells*				
Plating efficiency (%)	15–40	15–40	15–40	5–15
Dose range (Gy)†	2–6	4–10	4–10	4–10
No. of dose points analysed	4	4	4	4
$D_0 \pm 1$ SE (Gy)	0.78±0.12	0.90±0.05	0.92±0.02	1.13±0.07
$E \pm 1$ SE	6.1±6.0	11.9±4.8	17.4±3.5	4.9±1.9
(3) Survival parameters for SRUs, derived from curves of spheroid "cure"‡				
Dose range (Gy)†	2–6	3–7	5–8	5–9
No. of data points analysed	5	5	4	5
$D_0 \pm 1$ SE (Gy)	0.99±0.03	1.00±0.05	0.84±0.10	0.81±0.03
$LD_{37} \pm 1$ SE (Gy)	2.90±0.03	3.73±0.05	5.57±0.11	5.92±0.03
$\exp(LD_{37}/D_0) = NE \pm 1$ SE	18.7±0.5	41.7±2.6	770±150	1454±60
so that for the values of E in Section 2:				
$N =$	3.1±1.7	3.5±1.2	44±4	297±11
or, if a common D_0 (0.93±0.03 Gy) is fitted to all curves for clonogenic cells and SRUs, also yielding new values of E:				
NE (SRU) =	21.9±6.0	54.5±15.8	379±130	552±189
E (clonogenic cells) =	2.2±0.5	9.1±2.7	16.1±4.9	15.7±4.4
$N =$	10.0±1.9	6.0±1.6	23.5±3.3	35.2±3.9
cf. the expected range of numbers of clonogenic cells per spheroid (from Sections 1 and 2)	60–200	60–200	60–200	20–75

*Data for clonogenic cells are for three to six pooled experiments.

†Dose ranges were chosen to be approximately the same for the two methods of analysis.

‡Data for spheroid "cure" are for single experiments.

dividing the product NE for the SRUs by the independently determined values of E for the clonogenic cells, yielded numbers that in three of the four spheroid lines (VN, EE, MF) were lower than the estimated range of numbers of clonogenic cells per spheroid (Table I). For one line (GE) the derived number of SRUs was higher than that of the clonogenic cells, but lower than the number of histologically intact cells per spheroid. However, employing the common D_0, the numbers of SRUs per spheroid for all four lines were either lower than, or in the lower range of, the estimated number of clonogenic cells (Table I). Two possible explanations might account for this discrepancy. Firstly, that the values of E assigned are inappropriate for the SRUs. This could be tested by performing cure experiments with split doses of radiation. Secondly, that the probability that a clonogenic cell will also function as an SRU is less than unity. If all clonogenic cells are potential SRUs, some must be functionally destroyed *in situ* in the days following irradiation. The similarity of D_0 values for SRUs and clonogenic cells may indicate that such a post-irradiation "dip" would be independent of dose, at least over the present near-curative or curative range. The presence of a "dip" in the number of surviving clonogenic cells per spheroid might be detected by experiments in which the time of disaggregation of the spheroids is extended to intervals longer than the 18–24 h commonly employed.

In conclusion, careful experiments such as those of Rofstad et al (1986), using small spheroids of uniform size whose clonogenic cells have uniform sensitivity to radiation, suggest that the slopes of cure curves *can* be reconciled with the slopes of cell survival for the constituent clonogenic cells. Reasons for the apparent discrepancy of numbers between clonogenic cells and SRUs remain to be established.

Yours, etc.,
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Translumbar aortography

THE EDITOR—SIR,

I welcome the excellent articles by Jeans et al (1986a,b), as such in-depth analysis is invaluable in these cost-conscious days. However, I would like to comment on their use of translumbar aortography. They state (p. 458) that translumbar aortography was performed under general anaesthetic. Since the introduction of low-osmolality media, we have not found this necessary, although for certain departmental reasons, we have maintained one general anaesthetic session in the department. However, in 1985, out of 221 translumbar aortograms, 152 (68%) were carried out under local anaesthetic, using 10 mg diazepam 90 min before commencement, supplemented if necessary (about 10% of patients) by 5–10 mg diazemuls IV during the procedure. Patients who had had the examination under both general and local anaesthetic were questioned as to their preference. Ten per cent would have preferred general anaesthetic. The remainder were equally divided between those who preferred local anaesthetic and those who were indifferent. Therefore, I would suggest that translumbar aortography under local anaesthetic is highly acceptable, is an easy technique for trainees, and allows a one-day hospital stay for the patient. Cases examined before noon could go home the same evening if a day ward were being used which was open until 7 p.m. This must have a significant bearing on the costs of the examination and, therefore, Table II (p. 458) would, in our case, be modified to give a lower cost for translumbar aortography than that quoted for transfemoral aortography.

Yours, etc.,
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Proceedings of The British Institute of Radiology

The Assurance of Quality in Medical Imaging

Abstracts of papers presented at the above meeting, held at the Edward Lewis Lecture Theatre, Middlesex Hospital Medical School, London W1, on Wednesday, May 21, 1986

Session I: Quality—the systems approach

Chairman: Mrs M. J. Harvey

Evolution of quality systems in industry, by S. Stuart
The quality system applied to a medical imaging department, by I. R. F Hendra
The "customer's" view of quality in diagnostic imaging, C. D. Shaw

EVOLUTION OF QUALITY SYSTEMS IN INDUSTRY

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In ancient times quality was controlled by craftsmanship; industry was mostly small scale and consisted of many little local workshops controlled by master craftsmen who served local markets. There is no doubt that this system could produce products of high reliability and superb quality. It depended on many people of high inherent ability undertaking long training, as apprentices, to become craftsmen. It also depended on the master craftsmen knowing the needs of their local markets. Under this system manufacture was more of an art than a science, and technology evolved slowly. The craft system started to decay with the onset of the industrial and commercial revolutions of the 18th and 19th centuries. The status of the craftsman declined, from being his own master he became the servant of a large enterprise which was often controlled by financiers or others who had little regard for craftsmanship. The enterprise usually served distant markets and so his close contact with customers was broken. In modern times, products have become very complex and are based on science and technology which production workers do not understand. Technology changes rapidly.

Today the great majority of young people of high inherent ability go on to higher education and do not become production workers, and the average I.Q. of production workers has declined since World War II. Except in a few small luxury industries, craftsmanship is no longer an adequate method of controlling quality. In modern industry quality is assured by comprehensive management systems, such as are outlined in British Standard 5750. These systems place heavy emphasis on training, motivation, organisation, formal methods and procedures and similar concepts. Many of these concepts are of value in assuring quality in a medical imaging department.

THE QUALITY SYSTEM APPLIED TO A MEDICAL IMAGING DEPARTMENT

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Since quality systems are beneficial in commerce, the same should apply to medical imaging. The British Standards Institution publishes four handbooks on quality management systems. The books contain 60 British Standards. The cornerstone of the British National Quality Campaign is BS5750, *Quality Systems*, which can readily be applied to the manufacture of medical images in a hospital department. It describes general principles concerning the manner in which specified requirements are accomplished. These were described for an ideal image in order to provide the reference for the quality system. However, the key issues of BS5750 remain that quality assurance is dependent upon effective management and is the result of good liaison between users and producers. The BS5750 quality system requires full documentation of all the procedures involved in the production of images, together with planning, design control, manufacturing control, the control of procurement of materials and services and, very importantly, periodic objective reviews.

The place of equipment monitoring schemes (sometimes known incorrectly as quality assurance) and film reject analysis are described in the context of the BS5750 quality system. The former is included in the need to maintain equipment and therefore requires very close liaison with service agencies. The latter has no place unless it is clearly aimed at the need to correct unforced errors in procedure, is a permanent fixture and identifies all factors involved, including the identity of the operator. Applied even minimally, the BS5750 quality system would provide clear evidence that management is taking the necessary steps to ensure cost effectiveness and the use of minimum doses of radiation.

THE "CUSTOMER'S" VIEW OF QUALITY IN DIAGNOSTIC IMAGING

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Judgments on the quality of any element of health care depend on the criteria assumed to describe a "good" service. Some people judge in terms of adequate and equal access for the population, others in terms of technical effectiveness, or of user satisfaction, or of economy. The ideal service would meet all criteria but, in reality, legitimate views often conflict. Patients recognise diligence more than competence, they judge by comfort and courtesy rather than by whether a procedure is technically correct or even whether it is appropriate. Doctors who request examinations are also customers. They judge a service by its speed and effectiveness in narrowing the range of diagnostic doubt; but they may be unaware of the limitations of the examination or of the relative merits of alternative diagnostic tests. Many district departments now have "contracts of service", defining the staff, time and budget to be provided within individual units. The general manager thus becomes a customer, whose concern it is to make the most of limited resources across all departments, access and efficiency are more easily measured than quality and effectiveness.

In order to reconcile these conflicting views, it is necessary first to recognise that they exist and that they may be as legitimate as the department's perception of itself This could be helped by an explicit statement of expectations at local, regional or national level—"what is a good service?"—as hospital pharmacists have recently done. Or the professional bodies could follow the example of the Royal College of General Practitioners by defining a "good" radiologist or radiographer It might also be valuable to examine how far the Royal College's guidance on the use of diagnostic imaging has been applied in local practice. The customers recognise they are not competent to monitor technical quality, but they would be reassured to know that it is monitored by those who are.

Session II: Containing the risks through good practice

Chairman: Mrs M. J. Harvey

Radiation risk–benefit analysis, by J H E. Carmichael
Containing risks through equipment care, by J. A. Garrett and P. H. Smithson
Protocols for practical procedures, by O. Deaville

RADIATION RISK–BENEFIT ANALYSIS

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Quality control benefits the radiologist, the radiographer, the treasurer, the patient and the manufacturer (because he has a satisfied customer). One of the principal aims of quality assurance (QA) is to produce an image accurately and at the lowest radiation dose possible Therefore, there must be an element of radiation protection in QA. All doses matter to patients and staff: 90% of the man-made radiation dose received by the population comes from medical radiology and nearly all of that from diagnostic radiology. If QA reduces that dose then it reduces the stochastic effects to the population. Variation in output may mean repeating a film; too great a dosage demand at the input phosphor of an image intensifier will cause greater irradiation than necessary. The use of a phantom in checking mammographic technique (both for information content and dosage) is essential and as mass screening mammography on a national basis may well be recommended in the near future, it would be essential to test every technique used by a suitable QA system. Only then can one say that the technique is being carried out with the lowest possible dose and therefore with minimum risk to the patient.

Cost–benefit can be considered in respect of automatic exposure control equipment (in an attempt to reduce rejected films from exposure faults) and, in radiation protection terms, is cheap Applicability to a particular department would be assessed by the rejection-rate analysis of a QA programme Other cost–benefit analyses can be made in respect of carbon-fibre products (table top, bucky facing and interleaving, cassette facing). Quality assurance will show that there is no loss of quality and that there is dose reduction. The use of rare-earth screens will reduce dose and can be financed by saving on film costs again, QA testing will indicate to the user whether the screen–film combination being considered will lead to loss of information content The use of 100 mm film cameras would be cost effective if 7000 films a year were used. It should not be used as a supplement to large film but as a replacement for it. Quality assurance would tell a radiologist whether the information content was present on the film. If magnification was used to obtain an image, then again the information content and the dose rate should be checked, as dose may well be as much with a magnified image as with a full-sized film. Subjective impression may not give the true answer, hence the need for image information content to be checked with a phantom. The use of a diamantor, which measures dose and square area as a product, is a simple QA technique which helps train radiologists in good fluoroscopic practice. This will yield benefit over future years at a very cheap initial cost. Quality assurance is often used to check the efficacy of radiographic working practices. It should also be used to check that of radiologists.

CONTAINING THE RISKS THROUGH EQUIPMENT CARE

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The care of imaging equipment makes an important contribution to the assurance of quality of the imaging system product. Use of a data base designed to monitor the service performance of equipment is described. From the results so far it is possible to identify actions which might be taken to reduce the degree of system failure attributable to the imaging equipment. Areas identified include equipment design, engineering service and user care Examples are given of how modern designs can both contain the cost of manufacture and improve reliability. It is not envisaged that service costs will be reduced, since the more sophisticated equipment requires higher-calibre service techniques and personnel. However, it is possible that intelligent user care could reduce expensive engineer service calls.

PROTOCOLS FOR PRACTICAL PROCEDURES

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Practical procedures in medical imaging involve patients in a wide range of examinations which carry risks no matter how simple or complex the procedure. Limitation of these risks should be the aim of all those involved in any part of the procedure.

It is known that there are many recognised risks which are outweighed by the benefits to be achieved in undertaking the procedure. What must be minimised are those risks which have a definite adverse outcome and no benefit

What distinguishes a protocol from a code of practice or scheme of work? The Shorter Oxford Dictionary defines protocol in several ways These definitions relate to formal documents setting out the correct precedence to be followed These are recorded after discussion and agreement by all parties. Risk situations may not be identified until after the incident has occurred This then leads to an investigation and reprimand of staff involved Consideration must be given a more efficient and effective way of identifying risks .Three methods are proposed and discussed. (1) The formation of multiprofessional "buzz" groups in order that individuals may pool experiences and knowledge (2) Research of health authority records and literature relating to legal liability .This will reveal serious incidences of poor practice. (3) Monitoring of existing practice in departments to identify poor practice, corner-cutting and risk situations Protocols can then be designed to minimise these risks. The criteria to be followed are established and include the following aspects: (a) consultation and liaison between all professional groups, (b) agreement as to what is to be regarded as "good practice", (c) wording of the protocol to be concise and factual, (d) presentation and display, and (e) introduction and implementation. Later evaluation of the protocol, in practice, will ascertain its effectiveness and identify problem areas. Effectiveness, efficiency and acceptability (Long et al, 1985) in relation to the success of a protocol are discussed The aspect of efficiency raises a note of caution. "Could the introduction of rigid protocols for all practical procedures be seen by management as a way of standardising practice and limiting spending?"

The increasing evidence, as reported by Whincup, that practitioners have failed to comply with acceptable standards or failed to take reasonable care would indicate a need to formalise some procedures. The use of protocols for good practice could contain common known risks and form part of a quality assurance programme.

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Session III

Chairman: Dr P. Goddard

Ineffective imaging, by G. de Lacey
Equipment performance, by M. Fitzgerald
Communication and control, by F. A. Paris

INEFFECTIVE IMAGING

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A resumé is given of surveys produced during the late 1970s and early 1980s which assessed the clinical value of many routine radiological examinations. Almost all of these surveys have been comprehensively summarised and given very careful analysis in a 1983 publication from the World Health Organization (Technical Report Series No. 689: *A Rational Approach to Radiodiagnostic Investigations*). This interest in the assessment of the clinical usefulness of various imaging procedures has waned over the last few years, and one reason for this has been the explosion in new diagnostic techniques. Radiologists have necessarily had to spend most of their time mastering these techniques and dealing with the resultant increases in workload. Regarding efficacy surveys, disagreement between radiologists and between radiologists and other clinicians are highlighted and one example given is the place of skull radiography following a mild head injury. Some of the reasons for genuinely held differences in opinion are mentioned. These often relate to differences in defining the precise clinical circumstance and precise purpose for which skull radiography is utilised, and also to differences in economic evaluations of costs and benefits. Finally, the importance of continuing to initiate and carry out prospective evaluations of imaging protocols is discussed. Two examples are given in which a major change in common practice would appear to be sensible. Firstly: a routine urogram has been shown to be unnecessary in patients presenting with prostatic symptoms, though routine ultrasound should be performed in some 25% of these patients and some 10% of the latter will also subsequently require an intravenous urogram. It is emphasised that departments which have abandoned all routine imaging in patients with prostatism were arguably just as unwise as those who continue to perform routine urography or routine ultrasound in all such patients. Secondly, the value and place of ultrasound in screening children for congenital hip dysplasia (Berman, 1986, *British Journal of Radiology, 59*, p. 13) is given as another example in which ineffective X-ray imaging should be replaced by effective imaging.

EQUIPMENT PERFORMANCE

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One facet of quality control is equipment monitoring Its use in helping to achieve better equipment performance is discussed. Even in 1986, the subject has still to be considered because many authors have demonstrated that there is a wide variation in the performance characteristics of X-ray equipment; the patient may suffer unnecessary irradiation as a consequence, or may not be given enough and then the image may suffer. There is no agreed practical specification against which performance can be judged. Professional opinion, the ALARA principle (ICRP, 1977), Regulation 33 of *The Ionising Radiations Regulations 1985* (HMSO, 1985), the CEC directive on radiation protection of the patient (CEC, 1984), all support the argument for performance monitoring.

There are three phases to equipment monitoring (1) to specify the performance, (2) to test the performance of new equipment against the specification before accepting it, which for existing equipment amounts to status testing, (3) thereafter, regularly to monitor the performance. A new programme of monitoring should be preceded by an assessment of film rejects and of the dose received by patients for a selection of common X-ray examinations, these give a baseline against which future improvements can be set. It is the radiographer who should undertake the performance monitoring using simple, reliable, calibrated test equipment, which responds at clinically relevant exposure settings (Haywood & Ryan, 1985). The components of the imaging system should be tested separately and a set of test equipment could include a sensitometer, densitometer, radiation output meter and simple test tools for checking the light-beam diaphragm alignment, tomographic movements, film-screen contact and the noise, resolution and monitor settings of image-intensifier-television systems. The processor should be checked daily, the X-ray tube output weekly and other components less frequently. The performance of the processor and the radiation output of an X-ray tube should not vary by more than ±10%.

A plea is made for a collaborative approach to formulating performance specifications for the components of an imaging system. It is suggested that the DHSS could provide a strong lead by making available a set of test equipment to each health district in the country; this would cost under £300 000, which is very small in relation to the total cost of X-ray equipment.

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COMMUNICATION AND CONTROL

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This paper is presented under two main headings. Firstly, a description of systems operating within a hospital to enable a "machine history" to be kept for each X-ray and imaging room during its life time. Secondly, a discussion on communication between the user of the machine, the firm responsible for its maintenance and the manufacturer, with suggestions as to where improvements could be made in this chain

The control of quality. To monitor the performance of any X-ray unit, it is important that the department keep an up-to-date diary of its faults. This can be assimilated from: (1) the log book kept with each machine, in which should be recorded all faults as they occur, when the machine is repaired the service engineer should enter in the book the remedial action carried out, and (2) the service sheets completed when the engineer attends either for an emergency call-out or for a planned maintenance visit. Annually, a record of maintenance, breakdowns and their cost should be completed from the above paperwork. This information can be forwarded to the regional health authority and/or any relevant professional or national organisation, so that a record of history of multiple machines can be compiled.

Communication with suppliers and service agents. This can be difficult at times. To understand better each other's problems, radiographers and radiologists need some insight into engineering while engineers and service managers should also have an appreciation of clinical needs. Another perceived difficulty is that, in some instances, the sales department, the service department and the clinical support section of the organisation appear not to communicate with each other Add to this the fact that, although most service agents are based in the UK, many manufacturers of X-ray equipment are now in the United States or Japan. With the consequent communication difficulties both in time difference and language, it is not surprising that design and manufacturing faults occasionally take a long time to remedy. These difficulties are in no way insurmountable. Departments can be more observant as to what the machine is doing when an intermittent fault occurs; engineers can "sit in" on a clinical session; engineers can be given a "teach-in" on the equipment in the clinical situation; departments can have regular meetings with both the sales and the service side of the organisation. These are but a few ideas to maintain good working relationships between users of the X-ray equipment and its suppliers.

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Proceedings of the EORTC Heavy Particle Therapy Group

Abstracts of papers presented at the above meeting, held at The Douglas Cyclotron Centre and University of Liverpool Department of Radiation Oncology, Clatterbridge Hospital, Merseyside, on May 1–3, 1986

Edited by D. K. Bewley and R. D. Errington

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THE CHOICE OF MATERIALS IN A HIGH-ENERGY-NEUTRON FACILITY IN RELATION TO THE RADIATION HAZARDS TO STAFF

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Neutron-induced radioactivity presents a hazard to staff working with neutron therapy equipment that is not normally encountered in conventional radiotherapy. It is therefore of great importance that the problems of induced radioactivity be taken into account in the design of neutron therapy machines This, however, becomes difficult at high energies as there is a distinct lack of activation cross-section data above 20–30 MeV. For the new generation of high- energy neutron machines with energies in excess of 30 MeV recourse must be made to experimental data to assist in the choice of materials Materials for use in neutron therapy fall into two main categories. They are used either as shielding or for the manufacture of various machine components such as target housings, beam lines or other mechanical devices.

In order to determine which materials give the lowest levels of induced activity, various samples of approximately the same cross-section and volume were irradiated both at the cyclotron laboratory at Louvain-la-Neuve and at the Douglas Cyclotron Centre, Clatterbridge The neutron beams used were p(65)+Be(65) filtered by 5 cm of polythene and p(62)+Be(36) for Louvain and Clatterbridge, respectively. Samples were irradiated for 5 min and given a total dose of 50 cGy in tissue. The decay of the induced activity was then measured over a period of hours using an ionisation chamber-type dose-rate meter. At the same time small samples of material were also irradiated and the γ-ray spectra measured using a GeLi spectrometer Principal activation products were then identified and the decay of induced activity analysed using curve-stripping techniques. From the analysis of the decay curves it was possible to calculate the buildup of induced activity over several irradiations for each material.

The shielding materials considered were mild steel, stainless steel (ENJ58), pure iron, tungsten and polythene. Of the possible component materials, initially only titanium and stainless steel were considered, though recently phosphor bronze in comparison with stainless steel was investigated. With the exception of the latter investigation, which was made at Clatterbridge, all other samples were irradiated at Louvain-la-Neuve. The results show that the shielding materials with the lowest induced activity were pure iron and polythene. Significant differences were found between the various samples of iron, particularly between mild steel and pure iron due to the presence of ^{55}Mn contaminant Attix et al (1978) found no differences in induced activity in samples of iron irradiated with a d(35)+Be(35) beam. This difference in results is believed to be due to differences in the thermal neutron component of the beams and will be investigated further. The results also show that the component material with the lowest induced activity is titanium, however, if corrosion is not a problem then pure iron can also be used as a component material.

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TECHNOLOGISTS' EXPOSURES AND RADIATION PROTECTION ASPECTS OF THE CLINICAL NEUTRON THERAPY FACILITY IN SEATTLE

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The University of Washington clinical neutron therapy facility in Seattle consists of a 50 MeV proton cyclotron and two treatment rooms for neutron therapy One of the rooms is equipped with an isocentric gantry. The facility was designed to maintain leakage and remanent radiation as low as readily achievable and treatment equipment was specified with this goal in mind.

The design of shielding barriers and barrier penetrations was based on Report No. 51 of the National Council on Radiation Protection and Measurements (NCRP, 1977). Primary neutron-beam barriers are 2.5–2.8 m thick. Limestone (calcium-based) aggregate was utilised to minimise concrete activation via neutron reactions in ordinary silicon-based aggregate Tests showed that activation levels could be reduced by factors of 30 to 50 in the aggregates

The neutron production treatment unit is shielded with pure iron, boron-loaded polythene and lead. The patient support assembly is constructed of wood laminate, as is the movable floor which permits entry of the isocentric gantry below floor level. The automated built-in variable multileaf neutron collimation system and internal neutron-beam flattening filters and wedge filters obviate the need for handling of activated structures by the radiation technologists.

Measurements of the remaining activity in the treatment area immediately after treatment show a decay rate from about 30 mrem/h to 16 mrem/h on the beam axis in 10 min following beam shutoff Longer-range activation levels around the patient couch are 7–10 mrem/h.

Radiation technologists' monthly exposures during the first 18 months of operation have averaged 88 mrem with two or three technologists in service and treatment of 12–16 patients per day, 3 days per week. The average exposure per patient fraction (*i.e* treatment of slightly more than two fields per fraction on average) is approximately 1.6 mrem. This exposure is divided amongst the technologists in service.

REFERENCE

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RADIATION PROTECTION AT THE NEUTRON THERAPY FACILITY IN LOUVAIN-LA-NEUVE

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The radiation hazards to the neutron therapy staff at Louvain-la-Neuve have been evaluated During patient irradiation, the dose-equivalent levels in the treatment room were about 0 5 Sv h^{-1} and 0.7 Sv h^{-1} for the p(65)+Be and d(50)+Be neutron beams, respectively, assuming $Q = 10$ A long maze reduces the dose-equivalent level below 2 μSv h^{-1} at the room entrance. Induced radioactivity has also been studied. Immediately after patient treatment, the absorbed dose rate in the treatment room is lower than 0 2 mGy h^{-1}. The short-lived radionuclides created are mainly ^{53}F ($T_{1/2} = 8$ 53 min), ^{56}Mn ($T_{1/2} = 155$ min) and ^{52}V ($T_{1/2} = 3$ 75 min); as far as long-lived radionuclides are concerned, ^{54}Mn ($T_{1/2} = 313$ days) is the most important one. Since the target is automatically removed at the end of the treatment the absorbed dose rate on the beam axis is less than 0 3 mGy h^{-1}.

Whole-body dose equivalents to the neutron therapy staff recorded for 1978, 1979 and 1980, when d(50)+Be neutrons were used, were less than 10 mSv/year. After 1981, when p(65)+Be neutrons were used, these dose equivalents remained less than 15 mSv/year. For the therapists and radiographers the recorded dose equivalents can be correlated with the number of patients treated, resulting in a mean dose equivalent of 0.1 mSv per patient treated. Although these doses are higher than those for conventional radiotherapy they remain far below the recommended dose limits.

Activation in patients irradiated with p(65)+Be neutrons was measured. The radionuclides created were mainly short-lived positron emitters (^{11}C and ^{15}O). The activity, higher than 1.5 MBq 5 min after irradiation, could be visualised within the irradiation field at the PET camera, and could be used to check the accuracy of patient positioning.

DOSE EQUIVALENT DETERMINED BY TISSUE-EQUIVALENT PROPORTIONAL COUNTERS IN THE ENVIRONMENT OF THE NEUTRON THERAPY FACILITY AT LOUVAIN-LA-NEUVE

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Tissue-equivalent proportional counters (TEPC) are used in radiation protection to determine dose equivalent in an environment where unknown photon and neutron components are present. They measure the total absorbed dose as well as the linear energy distributions from which a mean quality factor ($\bar{Q}$) can be evaluated. The relationship $\bar{Q}$ vs LET (linear energy transfer, L) recommended by the International Commission on Radiation Units and Measurements and the International Commission on Radiological Protection to derive $\bar{Q}$ factors ($\bar{Q} = \int Q(L) . d(L) \; dL$) is used by adopting LET equal to the microdosimetric quantity y (lineal energy). This method of approximation can be used when the range of the secondary charged particles is large compared with the size of the sensitive volume, a condition which is fulfilled for neutrons of energy in excess of 100 keV.

The TEPC is particularly suitable to measure dose-equivalent in the environment of neutron therapy facilities. At Louvain-la-Neuve, a conventional "Rossi" counter 0.5 in diameter) was used to determine the y distributions on the axis of a p(65)+Be neutron beam, at 15 mm depth in a phantom The same detector was used to measure the dose equivalent in the treatment room and in the maze; the counter was exposed free in air with an additional buildup cap of 1 cm A-150 plastic On the beam axis, $\bar{y}_D$ (dose mean lineal energy) and $\bar{Q}$ were equal to 82.1 keV μm^{-1} and 7.3, respectively. They were equal to 37.7 keV μm^{-1} and 5.7 in the treatment room, and to 28.8 keV μm^{-1} and 4.1 in the maze. During therapeutic irradiations (proton beam of 12.5 μA), dose-equivalent rates were equal to 0.27 in the treatment room and 0.008 Sv h^{-1} in the maze. The relative γ contribution was estimated as equal to 0.04 on the beam axis; it increases up to 0.37 in the treatment room and up to 0.64 in the maze.

Portable TEPCs specifically designed for radiation protection purposes are being developed in several laboratories; these investigations are co-ordinated by the Commission of the European Communities and by the European Radiation Dosimetry Group (EURADOS) Portable TEPCs are being tested around the cyclotron at Louvain-la-Neuve.

THE PHYSICAL CHARACTERISTICS OF THE PRETORIA NEUTRON THERAPY BEAM

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The extraction system of the National Accelerator Centre cyclotron in Pretoria has been modified to deliver high-intensity deuteron-beam currents for radiation therapy. A fast-neutron field is generated via the d(16)+Be reaction on a thick target and is collimated by a variable-field-size collimator. Absorbed-dose measurements were performed in air and in a water phantom using a 0.5 cm^3 tissue-equivalent ionisation chamber (Exradin model T2) and an energy-compensated Geiger–Müller tube (Mullard ZP 1300). Both the intrinsic beam characteristics and the observed in-phantom measurements compare favourably with data obtained at other therapy centres with similar energies

Spectral energy measurements were undertaken to evaluate the ratio of the average energies required to create an ion pair (W_N/W_e) and the neutron kerma ratio $(K_t/K_m)_N$ Using NE213 liquid scintillator as a proton recoil spectrometer, the pulse shape discrimination technique was applied to determine spectra in air and in phantom Pulse height spectra were obtained at two gain settings under varying beam conditions and a well developed unfolding code (FORIST) was used to obtain the associated neutron spectra. W_N/W_e and $(K_t/K_m)_N$ were, respectively, calculated as 1063 and 0.991, while the mean neutron energy, $\bar{E}_n$, was determined as 6.33 MeV. These values are in good agreement with published data.

THE QUALITY OF THE PRETORIA FAST-NEUTRON BEAM

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To ascertain the quality of the Pretoria d(16)+Be fast-neutron therapy beam ($\bar{E}_n = 6.33$ MeV), three biological systems were irradiated using ^{60}Co γ rays as reference radiation

(i) V79 379A Chinese hamster fibroblasts, grown routinely in a monolayer culture, were irradiated during logarithmic growth and assessed for their prolific capacity Applying the multitarget model to the experimental data, survival curves were fitted by means of least-squares regression analysis and D_0 values used to calculate a mean RBE value of 1.7 Additional V79 dose–response data were analysed to verify the quality of the beam in terms of the linear quadratic model from an α–β scatter plot. The observed standard deviation relating to each experimental point was used to generate 127 sets of data according to a Poisson distribution and α- and β-values subsequently calculated in each instance. These simulated values were used to obtain the α–β scatter plot for comparison with a more comprehensive study.

(ii) Using an *in-situ* cloning technique, the survival response of jejunal crypt stem cells in whole-body-irradiated female CBA mice was determined Multiplicity corrections were applied to the number of crypts per circumference and the RBE calculated as a dose ratio at the 10-stem-cell survival level. An RBE value of 1.9 was calculated from this *in-vivo* assay.

(iii) Oxygen enhancement ratios for both ^{60}Co and fast neutrons were determined using *Vicia faba* 10-day growth and V79 hamster fibroblasts as end-points. The average value of 1.6 compared well with other published work.

Finally, measurements were performed to determine the recovery of V79 fibroblasts from sublethal damage After a recovery period of 3 h at 37°C, approximately 10% of the initially irradiated hamster cells remained viable. Top-up doses were then administered to complete the survival curves Recovery from sublethal damage, expressed as the $D_2 - D_1$ value at the 1% survival level, yielded 0.8 Gy and 3.2 Gy, respectively, for neutrons and photons.

The results obtained from the above assays did not suggest any marked dissimilarity in beam quality when compared with data from other centres using similar neutron sources.

THE CLATTERBRIDGE HIGH-ENERGY-NEUTRON FACILITY: SPECIFICATION AND PERFORMANCE

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The purpose of this paper is to present the results of measurements of basic performance of the Clatterbridge fast-neutron therapy facility in terms of both beam parameters and radiation protection. These results formed part of the acceptance tests for the machine.

The fast-neutron therapy facility consists of an MC-60 cyclotron manufactured by Scanditronix, Sweden and an isocentric treatment gantry manufactured by Elven Precision Ltd, England. The gantry has the capability of full 360° rotation but is at present limited to ±130°. Following acceleration to 62 MeV, the proton beam is extracted from the cyclotron and is transported to the treatment gantry, where it impinges on a beryllium target. Beyond the target is a flattening filter, a carousel containing three wedges with angles 20°, 35°, 45° and a variable collimator. The target isocentre distance is 150 cm and field sizes range from 5 cm × 5 cm to 30 cm × 30 cm. The target is beryllium with a composite backing of phosphor bronze, copper and water. The protons emerge from the beryllium with an energy of 26 MeV and are then stopped in 6 mm of the copper component of the backing. The measured total-dose output from the target is 1.63 cGy min^{-1} per μA at 150 cm SSD for a 10 cm × 10 cm field at the depth of dose maximum in a water phantom. The γ-ray contamination of the beam is 2–3% at the dose maximum.

Beam flatness is defined at a depth of 10 cm in a water phantom whose surface is at the normal SSD and is to be constant to within 3% over 80% of the field width for a 10 cm × 10 cm field. It was found necessary to use flattening filters to achieve this specification. One flattening filter is designed for fields up to a maximum of 16 cm. This combines with a second filter for larger field sizes. The beam penumbra in air for a 10 cm × 10 cm field at the normal SSD was found to be 13 mm for the 90% to 10% decrement lines. The 50% depth dose was measured for 5 cm × 5 cm, 10 cm × 10 cm and 20 cm × 20 cm fields and was found to be 13.4 cm, 16.2 cm and 18.8 cm, respectively. Measurements have also been made in the buildup region of the beam. For a 10 cm × 10 cm field at 150 cm SSD the depth of maximum buildup occurs at 14 mm in A-150 tissue-equivalent plastic.

Two aspects of radiation protection were evaluated, namely the shielding of the primary beam and the induced activity of the treatment unit. Measurements of the primary radiation leakage were made at a radius of 150 cm from the target. It was found that the shielding reduces the total kerma to less than 1% as far as 70° from the beam axis with 30–40% of this total due to neutron kerma. Beyond this the total leakage radiation rises to 3.5% (Bewley, personal communication, 1986). Studies of the buildup of induced activity over a 4 h period show a rise in activity in the region of the collimator to levels of approximately 150 μSv/h^{-1} 5 min from the end of irradiation, with a maximum of 320 μSv/h^{-1} to the rear of the target.

THE CLATTERBRIDGE HIGH-ENERGY-NEUTRON THERAPY FACILITY: MEASUREMENTS OF THE PARAMETERS OF THE CLINICAL NEUTRON BEAMS

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The radiation dose at any point within a phantom depends upon various beam parameters, in addition to the calibrated radiation output. Total-dose measurements of various beam parameters have been performed in a water phantom using ionisation-chamber techniques. Items specifically measured include: (i) depth-dose data for plain and wedged fields at various FSDs, (ii) buildup measurements for various field sizes and FSDs, (iii) profile curves at a range of depths for plain and wedged fields, and (iv) radiation output as functions of field size, wedge and FSD. The long-term stability of certain of these measurements has also been determined. Problems highlighted by them have included: (a) non-random fluctuations of dose owing to movement of the proton focal spot on the target, (b) non-applicability of equivalent square tables for wedged neutron beams, (c) deviations from inverse square law, particularly for FSDs less than 135 cm, and (d) unexplained fluctuations in the dosimetry calibration for large changes in ambient pressure. Each of these problems is subject to ongoing investigation.

The measurements outlined above have been entered into an IGE RT/Plan treatment-planning system to allow the production of standard isodose charts and individual treatment plans. These plans, charts, and variations of the individual parameters show similarities with 8 MV X rays produced by a linear accelerator.

THE CLATTERBRIDGE HIGH-ENERGY-NEUTRON FACILITY: DOSIMETRY INTERCOMPARISONS

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Both the requirement for meaningful exchange of clinical information between Clatterbridge and other high-energy-neutron facilities, and also the involvement in RTOG multicentre trials, have necessitated the performance of dosimetry intercomparisons with a number of centres with similar beam energies. Between July 1984 and November 1985 the following centres were visited for intercomparisons: Université Catholique de Louvain, Louvain-la-Neuve, Belgium; University of Washington, Seattle, USA; M.D. Anderson Hospital, Houston, USA, and Fermilab Cancer Therapy Facility, Chicago, USA. A return visit by the group from Louvain-la-Neuve to Clatterbridge facilitated a two-way intercomparison. The following procedure was adopted for each of the intercomparisons: (1) calibration of chambers in the home reference photon beam (^{60}Co), (2) calibration of chambers in the intercomparison centre reference beam, (3) neutron-beam measurements in a water phantom, and (4) application of protocol-dependent factors to obtain absorbed dose.

By performing the intercomparisons in this way, it was possible to obtain the overall difference in absorbed-dose measurements between the centres involved, while simultaneously locating the sources of any discrepancy. The overall difference was obtained as the product of the following ratios (participating centre/Clatterbridge): (a) the chamber responses in the neutron beam, using the intercomparison calibration factors, (b) the home/intercomparison calibration factors, and (c) the protocol-dependent factors required to obtain total absorbed dose from the chamber responses.

For the centres visited in the USA, overall differences of 1.5%, 1% and 1% were obtained for the University of Washington, M.D. Anderson Hospital and Fermilab, respectively. The most significant difference was obtained at Fermilab, where a +3% ratio in chamber responses partially cancelled with a −1.5% difference in calibration factors. For the two Louvain/Clatterbridge intercomparisons, overall differences of 1–2% were obtained, with most of the difference coming from chamber responses. It was concluded that although minor differences in the measurement of absorbed dose have been observed in this series of intercomparisons, the results indicate a level of agreement which provides a firm foundation for the exchange of clinical data.

NEUTRON ISODOSE DISTRIBUTION OBTAINED BY WEIGHTED MOVING-BEAM THERAPY

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Most neutron therapy facilities suffer from one or more disadvantages such as a fixed beam, unadjustable collimators and large neutron-producing targets of limited lifespan with a resulting larger penumbra. The subject of this presentation is a 14 MeV neutron generation with an unstable output and a penetration which is poorer than ^{60}Co γ rays and no skin-sparing effect. Thus we feel, as others do, that the full benefit of neutrons for the treatment of cancer will only be attained when these shortcomings are overcome through the design of better equipment and the development of more sophisticated treatment-planning techniques.

Current treatment-planning techniques developed for ^{60}Co and high-energy photons can result in inadequate and unacceptable neutron isodose distributions and they do not take into account the "neutron-specific inhomogeneity problem" where the energy deposition is highly dependent on the atomic composition of the tissues. We have approached this problem for our treatment facility by developing a computer-controlled treatment system to optimise dose distributions for 14 MeV neutrons with the feature that gantry angles and angular velocity can be continuously controlled to deliver the prescribed dose per unit angle corrected for the unstable output. Examples are given to compare dose distributions from weighted moving-beam therapy vs conventional treatment planning.

PROPOSAL FOR A MICRODOSIMETRIC INTERCOMPARISON BETWEEN EUROPEAN NEUTRON THERAPY CENTRES

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Biological properties of neutrons depend on the spatial distribution of discrete energy depositions by secondary charged particles; their spectrum varies with neutron energy, *i.e.* type and energy of incident particles, collimator structure and irradiation geometry. RBE ratios observed between neutron therapy beams used by different centres vary up to 30%.

By using tissue-equivalent (TE) proportional counters operating at low TE gas pressure, microdosimetry determines single-energy deposition distributions by charged particles crossing a volume of a few micrometres. This volume is negligible compared with the length of the particle tracks for the high-energy neutrons used in therapy and the microdosimetric quantity y (linear energy) can then be considered as an experimental evaluation of the LET.

Microdosimetric programmes were carried out by different teams at several neutron therapy facilities in Europe. Values of $\bar{y}_D$ (dose mean lineal energy) of 56.3, 74.2, 87.8, and 82.1 keV/μm^{-1} were derived for d(14)+Be neutrons (Essen), p(34)+Be neutrons (Orléans), d(50)+Be and p(65)+Be neutrons (Louvain-la-Neuve), respectively. Values of y^* (dose mean lineal energy corrected for "saturation") were derived and found to be 31.6, 28.4, 27.9 and 26.2 keV/μm^{-1}. For d+T neutrons (Hamburg), values of 81.1 and 25.9 keV/μm^{-1} were obtained for $\bar{y}_D$ and y^*, respectively. Observed RBE can be correlated with the y^* values.

It is of interest to repeat the measurements in similar conditions (same team, same detectors, same geometry). Therefore, a microdosimetric intercomparison will be carried out under the auspices of the EORTC Heavy Particle Therapy Group. A portable system is used to measure the microdosimetric parameters of the neutron beams, in reference conditions, at the facilities which are willing to collaborate.

CLINICAL EVALUATION OF EVENT-SIZE SPECTRA

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Microdosimetric investigations were performed in the collimated neutron beam at the Radiotherapy Department of the University Hospital at Hamburg. The 14 MeV monoenergetic neutrons are produced by bombarding a rotating tritium target with 500 keV deuterons (Franke et al, 1978). Event-size spectra were measured in different positions in a solid tissue-equivalent phantom (Schonka A-150) with a field size of 10 cm × 10 cm at 80 cm SSD. Proportional counters with different wall materials were used to separate the event-size distributions into the components of the different types of charged particles. As the RBE for damage in mammalian cells as a function of LET is known, the variation of the RBE with linear energy was determined from radiobiological measurement for crypt stem cells of mice (Zywietz et al, 1982).

With this RBE function the experimental event-size spectra are weighted so that mean RBE values are obtained for different positions inside and outside the useful beam. Finally, the influence of variations of radiation quality on isodose distributions was evaluated.

The calculations do not take into account the effects of low doses and different fractionation schemes and they are not valid for any biological system. The measurements and evaluations are helpful to estimate the biological efficiency of a neutron beam. This method can be used to compare different neutron beams with respect to RBE or to detect relative changes in the biological effectiveness of a neutron beam.

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RELATIVE BIOLOGICAL EFFECTIVENESS AS A FUNCTION OF NEUTRON ENERGY AND DEPTH IN PHANTOM

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Cell-survival studies have been performed with aerobic V79 cells *in vitro*. Both Hall and Cullen exposed cells at Clatterbridge in the autumn and winter of 1984 and 1985. On the first occasion exposures were made at two depths (2 cm and 12 cm) in a Perspex phantom and on the second occasion exposures were also made with a polythene filter. Hall's experiments were part of a series in which he is comparing the relative effectiveness of neutron generators in the USA and the

UK The result of the second experiment showed that the beam at Houston (42 MeV p on Be) is 6% more effective than that at Clatterbridge (61.5 MeV on Be). The beams at Cleveland, Seattle and Fermilab have been compared with one another but not with Clatterbridge or Houston The relative effectiveness of the beams does not correspond with expectation based on proton energy, but the discrepancies are reduced at a depth of 12 cm, suggesting that a low-energy component may have an important influence. Both Hall and Cullen found a small reduction at a depth of 2 cm when a polythene filter was used. These observations are, however, affected by the ratio of the mean dose received by the cells to the dose received by the chamber, a ratio which changed with depth and filtration When this is taken into account the results indicate a reduction of effectiveness at a depth of 12 cm of 2–4% relative to that at a depth of 2 cm and no change of effectiveness at a depth of 2 cm with the polythene filter It is concluded that further microdosimetric measurements are needed to interpret the results.

PRELIMINARY RESULTS OF A GEIGER COUNTER k_U MEASUREMENT IN THE CLATTERBRIDGE NEUTRON BEAM

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The presence of a γ-ray component in a clinical neutron beam complicates the derivation of a single dose–effect relationship based on the measurement of total (neutron plus γ) absorbed dose This is because of the different biological effectiveness of the two radiations, making it necessary to obtain an estimate of the proportion of γ radiation contaminating the beam The two-detector method is commonly used for this purpose, in which one detector is sensitive to both components of the beam and the other is relatively insensitive to neutrons. In order to measure a small γ component in the presence of a large neutron fluence, the neutron sensitivity (k_U) of the neutron-insensitive detector is required. At Clatterbridge preliminary measurements have been made using the lead-attenuation method to obtain the neutron sensitivity of two Geiger counters (type ZP1300). Attenuation data using lead absorbers were obtained for both Geiger counters and a tissue-equivalent chamber. The results were analysed using two methods. Firstly, the modified lead-attenuation method (Hough, 1979) was employed. Secondly, a curve-fitting method was employed, in which it was found that the Geiger attenuation data could be fitted by two exponentials and a constant component By assuming that the two exponential components represent attenuation of the neutron and γ components of the beam, it was possible to determine the proportion of the Geiger counter response due to neutrons, and consequently calculate the k_U value

k_U values for the two Geiger counters have been determined using these two methods, and a k_U enhancement has been demonstrated when Perspex instead of PTFE is used as the detector encapsulation, in agreement with the findings of other workers (Hough, 1979). Two methods gave results which were the same for the PTFE-encapsulated detector ($k_U = 4.9\%$) whereas for the Perspex-encapsulated detector, the first and second methods gave values of 5.2% and 6.0%, respectively. These values are in agreement with other centres with neutron beams of similar energy. Using these k_U values, estimates of the γ contamination in the Clatterbridge neutron beam have been obtained at various depths in a water phantom. The γ component as a percentage of the total dose is 2% for a 5 cm × 5 cm field at a depth of 2 cm, increasing with both depth and field size to a value of 6% at a depth of 20 cm for a 20 cm × 20 cm field. These values represent the two extremes of γ contamination in the clinical situation, and require clinical and radiobiological judgments of their significance.

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THE GAMMA COMPONENT IN CLINICAL NEUTRON BEAMS OF DIFFERENT ENERGY

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Neutron beams produced for therapeutic applications are always accompanied by a certain amount of γ radiation. Since the radiobiological characteristics of photons are different from those of neutrons an assessment of the γ component is neccessary. Neutron beams of different energies can be produced at the facility at Louvain-la-Neuve using protons with energies varying from 30 MeV to 85 MeV and deuterons with energies from 16 MeV to 50 MeV bombarding a beryllium target. An evaluation of the γ component was performed at different depths in a polystyrene phantom for seven clinical neutron beams: d(14.5)+Be (facility at Ghent), d(20)+Be, d(50)+Be; p(34)+Be; p(45)+Be, p(65)+Be and p(75)+Be.

Assessment of the photon contribution in a mixed field is generally made by the two-detector method, using a dosemeter which is relatively insensitive to neutrons, in conjunction with a tissue-equivalent chamber sensitive to both components. A Geiger–Müller counter (ZP1311+^{6}LiF cap) was used as the insensitive detector. The relative sensitivity (k_U) of this detector was measured previously by the modified lead-attenuation method. A linear increase in the k_U value with neutron energy was found for the neutron energies tested (Pihet et al, 1982). The k_U values used in the present study and derived from these data are 0.019; 0.019; 0.041, 0.028, 0.037; 0.061 and 0.071, respectively, for the seven neutron beams mentioned above

For the low-energy neutron beams the γ component shows a significant increase with phantom depth. from 5.3% to 21 3% for depths of 1.5 cm to 20.8 cm for the d(14.5)+Be neutrons and from 4.2% to 8 8% for depths of 1 5 cm to 11 cm for the d(20)+Be neutrons. For the high-energy neutrons, the γ component is small, slowly decreasing with neutron energy and slowing increasing with depth in the phantom, *i e.* for depths from 2 cm to 21 cm the γ component increases from 2.6% to 5 4%, from 5.4% to 12.1%, from 3.7% to 8 5%, from 3.4% to 6.0% and from 5 3% to 7.6% for the d(50)+Be; p(34)+Be, p(45)+Be, p(65)+Be and p(75)+Be neutrons, respectively

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COMPARISON OF NEUTRONS AT HAMMERSMITH AND CLATTERBRIDGE: RESULTS WITH MOUSE SKIN AND KIDNEY

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The biological effects of 60 MeV p-Be neutrons from the new MRC cyclotron at Clatterbridge were tested using acute (< 35 days) skin reactions on the feet of mice, and by assessing late kidney damage from 16–50 weeks after irradiation using decrease in ^{51}Cr-EDTA clearance and decrease in haematocrit as end-points. Radiation was given as one, two, four or eight equal fractions separated by more than 7 h. In the skin, 16 fractions were also given at Clatterbridge. Overall treatment time was 8 days for skin and 10 days for kidney. Low doses (< 1.4 Gy) per fraction were studied by administering eight equal fractions (16 for skin at Clatterbridge) followed by a top-up dose of 4 MeV d-Be neutrons.

For equal effects obtained at Hammersmith and Clatterbridge, we found the following. For skin a 9–16% dose increase was needed at Clatterbridge compared with Hammersmith, in the dose range 19–1.5 Gy per fraction (one to 16 fractions). At lower doses (< 1 Gy) per fraction, a 23–59% dose increase was needed at Clatterbridge. The best estimate for the limiting dose ratio at extremely low doses is 1.29±0.03. When measured relative to 240 kV X rays, the RBE for Clatterbridge neutrons rises from 1.6 to 4.8 as X-ray dose per fraction decreases from 29.5 Gy to 1 Gy. For kidney (at 31 weeks) a 21–40% dose increase was needed at Clatterbridge compared with Hammersmith, in the dose range 8.6–1.9 Gy per fraction. At doses ≤ 1.36 Gy per fraction, a 42–116% dose increase was needed. The best estimate for the limiting dose ratio at low doses is 1.9±0.15. At a Hammersmith dose of 1.47 Gy per fraction (the "standard" clinical dose expressed as neutron plus γ component and in line with the European dosimetry protocol) the ratio of Clatterbridge to Hammersmith dose for isoeffect was 1.12 for skin and 1.40 for kidney.

RELATIVE BIOLOGICAL EFFECTIVENESS FOR THE SPINAL CORD AT CLINICAL VALUES OF DOSE PER FRACTION

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The RBE for dose per fraction values in the clinical range, for 16 MeV d-Be neutrons relative to X rays, have been measured using a standard dose of neutrons or X rays followed by a range of top-up doses of X rays. The top-up doses of X rays required to produce myelopathy in half a population of rats was the same following 6 Gy of neutrons whether the neutrons were given in fractions of 0.5, 1.0 or 1.5 Gy over 3 weeks, showing that the isoeffect curve for neutron damage was flat over these values of dose per fraction. The isoeffect doses for X rays estimated from the X-ray fractionation data indicated that the isoeffect curve for X-ray damage below 2 Gy per fraction was at a lesser slope than that above 2 Gy; consequently RBE values derived from these data increase at a slightly lesser rate below 2 Gy per fraction of photons than above 2 Gy. The RBE relative to γ rays (using a factor of 1.1 to convert 250 kV X rays to equivalent γ-ray dose) at 2 Gy per fraction is 4.7, at 1 Gy per fraction, 6.4 and at 0.7 Gy per fraction, 7.2.

CHANGES OF QUALITY IN NEUTRON BEAM WITH DEPTH MEASURED BY JEJUNAL MICROCOLONIES

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The sensitivity of the mouse jejunum to neutrons from the Clatterbridge 60 MeV p-Be beam decreased by 11% when the mice were irradiated at a depth of 12 cm in a phantom compared with 2 cm, using the normal filtration and distance of patient treatment. When an extra 5 cm of polythene filtration was added the sensitivity at a depth of 2 cm was decreased by 8% but the sensitivity at 12 cm was unchanged. This suggests that the decrease in sensitivity with depth seen with normal filtration was largely because of low-energy neutrons which were filtered out by extra filtration or by depth within the phantom. The mouse jejunum was used because of its sensitivity to changes in LET. With less sensitive cell systems (see Bewley, Cullen and Hall) this change in sensitivity with depth was not detected.

THE EXPRESSION OF NEUTRON DOSE

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Neutron dosimetry is far from easy, both because of uncertainties in the assessment of absolute neutron dose and the problem of dealing with a wide spectrum of radiation quality, in particular the presence of γ rays in any neutron beam. The aim in dosimetry for neutron therapy is to express the dose in such a way as to provide the best predictor of biological response. In recent years it has become clear from radiobiological studies that at the dose levels normally used in neutron therapy (1–2 Gy per fraction), where the contamination by γ rays will normally be in the range of 5–40 cGy, the biological effectiveness of these γ rays is almost negligible. Thus, the neutron (or high LET) part of the dose will more accurately predict the biological response than will the total dose. Indeed, the use of total dose can be extremely misleading, for example in making intercomparisons between centres or even comparing treatments for lesions at different depths using the same facility. Measurement of the neutron dose requires subtraction of the γ-ray component, which introduces a substantial uncertainty in the estimation of neutron dose. However, this is now possible with reasonable accuracy and it is argued that the use of neutron dose, including the uncertainties in its measurement, is preferable to the use of total dose.

BIOLOGICAL IMPORTANCE OF GAMMA-RAY CONTAMINATION IN NEUTRON BEAMS

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Experimental information on this subject at levels of dose per fraction used in radiotherapy is meagre. One of the most relevant papers on the subject is that of Joiner et al (1984), who measured skin reactions in mice irradiated simultaneously with neutrons (4 MeV d on Be) and 140 kV X rays. They used one to eight fractions, at two fractions per day, and covered a range of doses per fraction. They analysed their results by the linear-quadratic model in order to obtain the parameters of the underlying cell-survival curves. I used these parameters to calculate the RBE of the X-ray components at 2 Gy per fraction when the neutron component was reduced from 100% of the total to 90%, 80% and so on. This indicated that small additions of X rays have an RBE of 0.2 relative to the neutrons. The calculation was extended to mixtures of γ rays in the Clatterbridge neutron beam by allowing for an RBE of 1.15 for 140 kV X rays relative to γ rays and an RBE of 3 for Clatterbridge neutrons relative to γ rays at 2 Gy per fraction of γ rays. The RBE of small additions of γ rays was found to be 3.2 Thus, these experiments and analysis do not suggest a very low effectiveness of a small contribution of γ rays in the Clatterbridge neutron beam.

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RADIOBIOLOGICAL INTERCOMPARISON OF NEUTRON BEAMS USED FOR CLINICAL APPLICATIONS

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The growing number of neutron therapy centres makes it necessary to compare the radiobiological properties of the beams systematically in order to interpret the clinical results. This paper summarises the results on RBE obtained for different neutron beams with energies covering most of the range presently used in the world for clinical applications.

Regeneration of intestinal crypts in mice, 3.5 days after total-body irradiation in a single fraction (Withers technique), was used as the biological criterion. The reported RBE values correspond to the regeneration of 50 crypts per circumference The animals (13 weeks old NMRI mice) were irradiated at a depth of 5 cm in a polystyrene phantom, with a dose rate of 0.2 Gy mm^{-1}. The doses were determined according to the ECNEU protocol and the experiments were performed by the same team, using similar irradiation techniques.

A first set of experiments was performed at the variable-energy cyclotron "CYCLONE" at Louvain-la-Neuve in Belgium, with neutron beams produced by 34, 45, 65 and 75 MeV protons bombarding a 17 mm-thick beryllium target (2 cm additional polythene filtration) and by 50 MeV deuterons bombarding a 10 mm-thick target. Taking as reference the p(65)+Be neutrons at a dose level of 7.8 Gy, RBE values of 1.12±0.07, 1.07±0.07, 1.00 (reference) and 0.96±0.06, respectively, were found for the different beams produced by protons; the RBE of the d(50)+Be neutrons was 1.02±0.07.

A second set of experiments was performed at other facilities with lower-energy neutron beams. Ghent (Belgium) for d(14.5)+Be and Riyadh (Saudi Arabia) for p(26)+Be (4 cm additional polythene filtration). At both centres, the radiobiological experiments were combined with a dosimetry intercomparison; the ^{60}Co γ-ray response was verified for radiobiology as for dosimetry. Using again p(65)+Be neutrons as reference, RBE values of 1.46±0.14 (Ghent) and 1.21±0.12 (Riyadh) were obtained

In conclusion: (1) the RBE for intestinal crypt regeneration increases to up to 40% with decreasing neutron energy in the "clinical" range; (2) present values indicate a steeper variation of RBE with neutron energy than the data reported on mammalian cells *in vitro* by Hall and Kellerer (1979), but a smaller RBE variation than the data obtained previously in our laboratory with *Vicia faba*; and (3) a single "average" RBE value is then not sufficient for comparing neutron data between one centre and another

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MITOTIC DELAY AND ITS VARIATION WITH THE AGE OF THE CELLS, AFTER X-RAY AND FAST-NEUTRON IRRADIATIONS. A TIME–LAPSE CINEPHOTOMICROGRAPHIC STUDY

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The mitotic delay of EMT6 cells irradiated with 250 kV X rays and fast neutrons was studied using a time-lapse cinephotomicrographic technique. The neutrons were produced by the cyclotron "CYCLONE" at Louvain-la-Neuve in Belgium by bombarding a 17 mm-thick beryllium target with 65 MeV protons

EMT6 cells (2.5×10^4) were plated into 25 cm^2 flasks ("Waymouth" medium+20% fetal calf serum) and were exposed to increasing doses of radiation at the time of their third generation (48 h after trypsinisation) The pedigree and cycle duration of each cell were determined by following its divisions on a television screen after the films had been transferred to videotapes. In order to facilitate this analysis, the real time (h, min) as well as the temperature were simultaneously printed on each microscopic frame at the moment of shooting, by means of an original "optical incrustation system".

In exponentially growing cell cultures, the median cycle duration of unirradiated cells was equal to 9.50±0.06 h and remained constant during five generations. After X irradiation, the median cycle duration of the irradiated generation reached 10.87±0.33, 12.90±0.63, 13.12±1.12, 14.88±0.83, 16.85±0.92, 16.75±1.15, 16.58±1.40 and 17.90±1.26 h for doses of 1, 2, 3, 4, 5, 6, 7 and 8 Gy, respectively; after neutron irradiation, it reached 11.43±1.10, 13.22±0.66, 15.48±0.99, 15.32±1.09 and 18.25±0.64 h for doses of 0.75, 1.50, 2.00, 2.50 and 3.50 Gy, respectively. For both radiation qualities, these values are compatible with a linear increase in mitotic delay with dose, at the rate of 1.30±0.30 h Gy^{-1} for X rays and 2.52±0.40 h Gy^{-1} for neutrons. The neutron RBE for mitotic delay is then equal to 1.9. It differs from the value of 2.6 obtained for the lethality of the same cells after 2 Gy "equivalent" irradiation. This implies that, for the same lethality rate, the cell age distributions after X rays and fast neutrons are different.

Mitotic delay also depends on the age of the cells in the mitotic cycle at the moment of irradiation. For both radiation qualities, it is larger in the radiosensitive phases: it increases from 1.3±0.3 h Gy^{-1} in late S to 1.9±0.3 h Gy^{-1} in early S for X rays, and from 2.3±0.5 h Gy^{-1} in late S to 2.8±0.4 h Gy^{-1} in early S for neutrons.

IS THERE POTENTIAL FOR SELECTIVE NEUTRON RADIOSENSITISATION?

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This paper sets out to evaluate the possibility that a selective neutron radiosensitisation of malignant cells may be achievable. In the past, the majority of work on neutron sensitisation has centred on the ability of ^{10}B to capture neutrons in the thermal energy range with the subsequent emission of an α particle. Such a highly destructive particle of short track length (9 μm) is appealing in that selective targeting of ^{10}B, by conjugation to a carrier such as an antibody and subsequent neutron irradiation, should result in highly localised cell destruction.

Owing to geometric considerations, delivery of ^{10}B to target cells is desirable in such a way that uniform distribution throughout the cell is achievable as opposed to localisation to the cell surface or an intracellular compartment. As a model system HT29/5 colonic adenocarcinoma cells were exposed to boric acid at 100 μg/ml, which had proven to be non-toxic to the cells *in vitro*. Following subsequent thermal-neutron irradiation it was determined that extended exposure of cells to ^{10}B from 1–6 days did not lead to a cumulative effect and that rigorous washing of cells with ^{10}B free culture medium 1½ h before irradiation resulted in a complete loss of radiosensitisation. These observations suggest that selective delivery of ^{10}B in a free form and its subsequent retention within tumour cells will be difficult to achieve owing to the ability of the material to move with ease across the cell membrane. Conversely, delivery of ^{10}B in a poorly diffusable form will presumably result in its localisation to a lysosomal compartment at best. Such a restriction would significantly increase the amount of ^{10}B required per cell to affect cell killing.

Calculations performed by Fairchild et al (1985) to determine the maximum amount of ^{10}B which could be delivered to a tumour using antibody-directed targeting were analysed and found to be overoptimistic. They assumed 10^6 antigens per target cell, 10^3 ^{10}B atoms per antibody and 1000 μm^3 as the approximate cell volume By this calculation the maximum achievable ^{10}B concentration would be of the order of 17 μg/g of tumour tissue, very close to a therapeutically useful level. Recalculation of this figure using recent data on the level of antibody localisation achieved in the clinic lead to a much reduced theoretical maximum ^{10}B concentration in tumour. Assuming 0.001% injected antibody per g of tumour (Kempshead), 10^3 ^{10}B atoms per antibody, 1000 μm^3 as the approximate cell volume, and 1 mg total injected antibody, resulting in a concentration of 71 ng/g.

In response to these observations, work has commenced in this laboratory in an effort to achieve selective radiosensitisation of tumour cells using a conjugate of an antibody linked to a conventional radiosensitising agent, initially bromodeoxuridine (BrdU). Results presented demonstrate a clear advantage of this system, in that BrdU has the ability to radiosensitise cells to both photon and fast-neutron irradiation, making it a much more widely applicable concept. The relatively long time course of clearance of non-localised antibody results in optimum tumour/normal-tissue differential occurring between 2 days and 4 days after administration (Moshakis, 1981). BrdU is appropriate for our model system in that it relies upon insertion and retention within the target-cell DNA for the exertion of its biological effect. This retentive nature may prove important in these studies By activating the BrdU 4 days after administration, thereby allowing time for clearance of non-localised material, a high degree of selectivity of radiation damage may be achievable in this system.

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FAST-NEUTRON THERAPY IN PELVIC MALIGNANCY

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Three trials of fast-neutron irradiation have been conducted in Edinburgh in patients with pelvic tumours. One hundred and thirteen patients were recruited to the trial on bladder cancer, in which patients with all stages of disease were included. Fifty-three were randomised to neutron therapy and 60 to photon therapy The overall local tumour regression rate was similar in the two groups with 64% of the neutron-treated patients and 62% of those receiving photons achieving complete tumour regression. Similarly, recurrence rates were found to be equivalent in the two groups. The persisting overall local tumour control was 43% in both treatment groups and was related to the T classification However, serious late complications were seen much more frequently in those patients who had received neutron therapy. Twenty-four of these patients had severe late radiation reactions in the bowel which, in 16 cases, directly contributed to the death of the patient. In contrast, six patients treated with photons had serious morbidity which proved fatal in two. Twenty patients in the neutron group and 15 in the photon group suffered severe late bladder reactions. The late morbidity following neutron therapy was first observed approximately 9 months after the start of treatment. The difference in morbidity in the two groups was highly significant statistically ($p < 0.001$). This led to a significantly poorer survival in the neutron-treated group compared with that in the photon-irradiated group. Again the difference in survival is highly significant ($p < 0.001$)

Two randomised trials of neutron therapy in rectal adenocarcinoma were performed, one in patients with inoperable tumours and the second in those with post-operative recurrent disease. There was a combined entry of 77 patients into these trials. Local tumour control rates were the same in both groups. However, morbidity occurred with greater frequency in patients treated with neutrons Survival was also seen to be different in the two arms of the study. In the inoperable trial the 2-year survival was 10% following neutron therapy and 43.6% following photon therapy In the recurrent trial the corresponding survival figures were 13.3% and 31.3%, respectively From these trials of pelvic cancer it is concluded that fast-neutron therapy has no advantage when compared with photon therapy when neutrons of the energy available in Edinburgh are used.

MEASURING AND RECORDING OF TREATMENT MORBIDITY

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In the assessment of any new method in radiotherapy designed to improve the rate of cure, normal-tissue reactions, acute and late, must be monitored with as close attention as the effects upon tumour. Careful observation needs to be made and normal-tissue effects quantified, but there is no scheme for the grading and recording of such morbidity which is generally followed. The recommendations of the World Health Organization *Handbook for Reporting the Results of Cancer Treatment* are widely accepted for the recording of reactions due to cytotoxic chemotherapy. This publication is, however, largely concerned with acute reactions and very little attention is given to the chronic and late effects which are so important in radiotherapy. An RTOG/EORTC scheme for the recording of late effects has been devised and tends to be used in some, but not all, studies performed under the supervision of those organisations. Table I shows the results of a limited survey of papers published in 1985 in American and European journals concerned with radiotherapy. The results confirm the lack of standardisation in the recording of morbidity.

A great deal of attention needs to be given to the establishment of international standards for the recording of radiation morbidity. Such morbidity is particularly important where the pattern may be altered from that seen conventionally, either because a combination of methods is being employed, such as the addition of a cytotoxic drug, or where the pattern to be expected differs from that seen conventionally, such as with neutrons One approach to the measurement of chronic or late damage is to use simple quality-of-life criteria. In this way morbidity at different sites can be given a grading relating to the importance to the patient

TABLE I

THE DESCRIPTION OF MORBIDITY IN PAPERS DESCRIBING THE RESULTS OF RADIOTHERAPY PUBLISHED IN 1985

	US-based journals	European-based journals	All (%)
Total examined	58	25	83
Radiation morbidity			
not mentioned	11	5	16(19)
mentioned but no data	8	2	10(12)
case descriptions only	19	8	27(33)
incidence figures but no scale of severity used	12	3	15(18)
"local" scale of severity	5	5	10(12)
EORTC/RTOG scale	2	2	4(5)
other published scale	1	0	1(1)

rather than to the particular system or tissue involved The Cancer Therapy Committee of the MRC has proposed a small international workshop in order to make advances in this field.

THE BENEFICIAL AND ADVERSE EFFECTS OF 7.5 MeV NEUTRONS

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The beneficial effects of 7.5 MeV neutrons in 207 locally advanced (T_4 N_{0-3}) tumours were a high control rate (74%) and a median survival of 32 months. Most tumours regressed rapidly, giving reduction in symptoms from the first treatments. In salivary-gland tumours the function of the VII nerve was maintained or regained in 77% and disfiguring surgery was avoided in cases of paranasal-sinus and oral-cavity tumours. Eroded mandibles repaired after neutron therapy in 45% of cases. Adverse effects were skin necrosis in 21% of 179 patients not previously irradiated and damage to other tissues in 8%. Where previous irradiation had been given there was major necrosis in 21%. These low-energy neutrons give no sparing of the skin Many of the skin complications will be reduced with higher-energy neutrons. There were other major difficulties with poor penetration of 7.5 MeV neutrons and with the fixed horizontal beam and restricted numbers of field sizes

Even using a primitive machine, which added significantly to complications, results were strikingly better than could have been expected from other treatments: indeed, some patients had already received multiple treatments. Sixteen years ago the results of combination chemotherapy for advanced Hodgkin's disease were reported (Devita et al, 1970). Eighty-one per cent of 43 patients completely responded and their median survival was 29 months. These patients were not in a controlled trial, but chemotherapy was accepted as the treatment of choice and an important advance was made. With the dose and techniques used, neutron therapy was as optimal a treatment for the advanced tumours we have described as chemotherapy appeared to be in 1970 for advanced Hodgkin's disease. To demand verification by controlled clinical trials with all their uncertainties seems unrealistic and not in the best interest of patients.

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REVIEW AND ASSESSMENT OF A CLINICAL NEUTRON THERAPY SYSTEM: EQUIPMENT DESIGN AND ENVIRONMENT

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The University of Washington fast-neutron beam radiotherapy programme has evolved through two major phases. In the first phase, a facility was developed at the U.W Physics Laboratory's fixed-energy cyclotron utilising the d(21)Be(15) reaction (Wootton et al, 1975). The resultant fast-neutron beam was shaped by interchangeable fixed collimators individually constructed to reproduce the required treatment fields Organ blocking was achieved with iron shields supported from the front face of the primary collimator. Treatment beams were simulated by a light localiser, and patient position could be monitored by direct television viewing of laser-light locating beams. An X-ray-port filming system confirmed fields. A treatment chair suspended from an overhead gantry was convertible to a standing, kneeling or horizontal lying device. The *x*, *y* and *z* movements were motorised Dose rates of 35 cGy/min in tissue were available at 150 cm from the targets Fifty per cent depth dose was achieved at 9 cm in a 10 cm × 10 cm field. D_{max} occurred at a depth of 2 5 mm. Beam profiles in the penumbra were better than those of ^{60}Co and similar to those of a Mevatron 8 Patients were treated on that facility from autumn 1973 to summer 1983.

In the second phase a Scanditronix MC50 cyclotron was combined with proton-beam transport and a neutron-beam collimation control system with separate fixed and isocentric gantries, treatment head and patient support systems (Elven Precision Ltd). A p(50)Be(25) reaction was used to generate a fixed horizontal neutron beam in one room and an isocentrically mounted beam in the other. A requirement for 360° rotation and a continuously variable multileaf collimator for the isocentric gantry, a moving floor to admit the treatment head below floor level and X-ray-port filming capability for both heads were included. The resulting facility provides fast-neutron beams having dose buildup, depth dose and penumbra characteristics almost identical to those of a 6 MV photon beam The continuously variable multileaf collimator delivers complex field shapes without the need for individual field blocking (Brahme et al, 1983) The direct X-ray porting verifies these complex fields.

This facility has been in clinical operation for 18 months to date, with three treatment days per week (Tuesday, Wednesday and Thursday). Scheduled maintenance is conducted on Monday, beam research and development Friday to Monday. Operational reliability (*i e.*, patients treated vs patients scheduled for treatment on a given day of normal operation) over the past 18 months of operation has averaged 92% and over the last 6 months has risen to 94% Subsystem failure rates can be attributed to cooling systems (19%), therapy gantry, collimator and patient support assembly (18%), ion source (9%), magnet (8%), and vacuum systems (8%).

Cyclotron time has been distributed among therapy (63 6%), physics (9 6%), scheduled maintenance (19.1%), unscheduled maintenance (5.9%), and outside users (1.86%). Isocentric gantry angles used to treat 150 patients are 90°, 270° (30%), 0° (25%), 110°–180° (*i.e* floor open) (30%) and 0–110° ≠ 90° (15%) These data are similar to those for our four LINAC X-ray machines. All patients have been treated on the isocentric unit

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FAST-NEUTRON RADIOTHERAPY FOR LOCALLY ADVANCED PROSTATE CANCER: RESULTS OF A RADIATION THERAPY ONCOLOGY GROUP RANDOMISED STUDY

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Between June 1977 and April 1983 RTOG sponsored a Phase III randomised study comparing the efficacy of mixed-beam (neutron/photon) radiotherapy with conventional radiotherapy for patients with locally advanced (Stages C and D1) adenocarcinoma of the prostate gland Patients received 50 Gy-equivalent whole-pelvis irradiation followed by a 20 Gy-equivalent boost to the prostate bed and any other areas of gross disease A total of 91 analysable patients were entered into the study, 78 of them being treated without major deviations from protocol. The two treatment groups were balanced in regard to all major prognostic variables (age distribution, tumour grade, stage, method of diagnosis, percentage of patients having lymphangiograms, laparotomies, or other methods of nodal evaluation, serum acid phosphatase levels, degree of seminal vesicle involvements, Karnofsky performance status, prior hormonal therapy status, cardiac disease status and Gleason score). At the time of initial analysis, the median follow-up time was 54 months (range 14–80 months). At that time actuarial curves for overall survival, plus determinantal plus survival, and local/regional control showed an improvement in treatment results in the mixed-beam subgroup. The local/regional tumour recurrence rate was 7% for the mixed-beam group compared with 22% for the photon-treated group at 5 years. The overall 5-year survival rate was 62% for the mixed-beam group compared with 35% for the photon-treated group These differences were statistically significant at $p \leqslant 0.05$. A more recent analysis with a median follow-up time of 80.5 months (range 40.8–108.0 months) continues to show a definite benefit to the mixed-beam form of treatment. At 7 years actuarial plots show a local failure rate of 20% in the mixed-beam arm compared with 70% for the photon arm and a survival rate of 68% for the mixed-beam group compared with 28% for the photon group ($p \leqslant 0.01$). This is the first randomised study showing improved benefit to fast-neutron radiotherapy for a specified patient group It also demonstrates that improved local control can favourably affect survival for prostate cancer

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CLINICAL RELATIVE BIOLOGICAL EFFECTIVENESS, INSTITUTIONAL RELATIVE BIOLOGICAL EFFECTIVENESS, CLINICAL NEUTRON POTENCY FACTOR

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The RBE of a given fast-neutron beam compared with γ rays varies with dose and biological system or effect. Among the observed RBE values, the most relevant from the point of view of neutron therapy is the RBE for late effects on normal tissues. The clinical neutron potency factor (CNPF) can be defined as an "average" or "overall" RBE of a given neutron beam relative to γ rays for late effects on normal tissues and a standard fractionation (2 Gy per fraction for γ rays) The neutron dose multiplied by the CNPF is the photon equivalent dose. When designing therapeutic protocols, the dose level in the neutron arm is then obtained by dividing the prescribed target absorbed dose in the photon arm by the CNPF However, a correction factor ${}_\gamma C_{fr}$ has to be applied if the adopted fractionation scheme for photons differs from the standard fractionation (2 Gy). Similarly, a correction factor ${}_n C_{fr}$ has to be applied if the adopted fractionation scheme for neutrons differs from the standard fractionation (2 Gy "equivalent"); ${}_n C_{fr}$ is, in general, close to unity.

When selecting the neutron target absorbed dose, an additional factor has to be introduced, $g_{n/\gamma}$, to take into account differences in physical selectivity between photon and neutron irradiation, to the extent that they influence the late tolerance. With the introduction of high-energy cyclotrons, this geometry factor $g_{n/\gamma}$ will come closer and closer to unity. As a matter of fact, the beam penetrations are improving and similar beam arrangements will be chosen more and more frequently for neutrons as compared with photons.

If D_n and D_γ are prescribed target absorbed doses for fast neutrons and γ rays, respectively:

$$D_n = D_\gamma \,.\, 1/(\mathrm{CNPF}) \,.\, {}_\gamma C_{fr}/{}_n C_{fr} \cdot g_{n/\gamma}$$

The expression "clinical RBE" or "institutional RBE" has been used to designate the ratio of the photon and neutron doses (D_γ/D_n) in therapeutic protocols. This ratio is not an RBE in the strict sense and it includes, in particular, the factor $g_{n/\gamma}$ which, in a given institution, varies with tumour location When normal tissues are irradiated for which the RBE is known and significantly higher than the average RBE for late effects (such as the central nervous system), the tolerance dose for the neutron protocol has to be calculated using, not the CNPF, but (when available) the actual RBE value for that particular tissue and the applied fractionation

FACILITIES AT THE KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE FOR A NEUTRON THERAPY PROGRAMME

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The King Faisal Specialist Hospital and Research Centre (KFSH & RC) in Riyadh incorporates the major cancer centre in Saudi Arabia, an advanced facility for research and treatment of cancer It includes a TCC (The Cyclotron Corporation) CS-30 cyclotron-based isocentric neutron therapy unit Model 4000 which became operational in late 1983, with the first patient being treated in January 1984. This model is believed to be unique in the world since it was modified to produce neutrons with the p(26)+Be in addition to the d(15)+Be reaction Using proper filtration (4 cm 10%

lithiated polythene filter) the neutron beams from both reactions were investigated in terms of beam penetration. For a 10 cm × 10 cm field, the 50% central-axis depth dose for $d(15) + Be$ neutrons was at 9.2 cm, while that for $p(26) + Be$ neutrons was at 10.4 cm, thus justifying the use of the latter reaction in this institution. The above modification qualified the unit as a medium- rather than low-energy neutron therapy machine, thus leading to potential reduction in the rate of complications. The isocentre of the unit is located at 125 cm and the corresponding dose rate at maximum proton current ($50\ \mu A$) in water for a 10 cm × 10 cm field is 13.8 cGy/min. Recently, physical and radiobiological intercomparisons were performed in collaboration with the Université Catholique de Louvain, Brussels, Belgium, and the preliminary results showed good agreement between the two institutions. These intercomparisons were very much needed to evaluate the clinical quality of the neutron beam and to enter into collaborative studies with international neutron-therapy centres. It will provide a new impetus to the neutron therapy programme at this institution.

AN INTERIM ASSESSMENT OF MIXED-SCHEDULE TREATMENT IN UTERINE CERVICAL CARCINOMAS

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Locally advanced cervical carcinomas are frequently hypoxic and conventional treatment leads to a low control rate. Therefore a fast-neutron therapy trial seemed to be feasible. The results of a Phase I study performed in Orléans in 1983 and those published by NIRS in 1982 and RTOG in 1983 led us to start a Phase II trial. Thirty-six patients were studied: 26 Stage IIIb and 10 Stage IVa. The first course of treatment was similar for all patients, and used a mixed schedule delivering 50 Gy eq. γ over 5½ weeks to the whole pelvis. The second course, performed after a rest period of 8–15 days, consisted of a boost to the primary tumour site, for 31 patients with an intracavitary application and for five who had had external-beam irradiation.

Of 19 patients with persisting local control, 16 are still alive (median survival 16 months) and three are dead (one of intercurrent disease, two of metastases). Of 13 patients with local failure, seven are still alive (median survival 14 months) and six are dead (median survival 10 months). For the last four patients, we know only that two are alive and two are dead. Local control can, therefore, be evaluated on 32 cases.

At 30 months, local control is about 60% for the whole group and a quite good survival rate is observed, but a highly significant difference in survival can be seen between two groups of patients: TIII, 92% at 2 years, and TIII with ureteral obstruction and TIV, 28% at 2 years. The excellent survival rate of the TIII group might be because of a bias in patient selection. For more than 80% of the patients no complication ever appeared. Most of the complications had no durable functional repercussion; only sclerosis persisted and in one case this required a colostomy. Local failure remains the main cause of death.

Current results concerning neutron therapy for advanced cervical carcinomas are disappointing. For this, two hypotheses can be formulated: cervical carcinomas are relatively rapidly growing tumours, thus the possible benefit of neutrons to the anoxic part of the tumour is cancelled; or, the level of neutron dose is too low, compared with the total dose (30% for American and Japanese studies, 50% for our study). In that respect, it might be useful to modify our treatment scheme. This could be realised either by increasing the neutron dose level or, as proposed by Maruyama, by using californium for the intracavitary application.

NEUTRON AND NEUTRON-BOOST IRRADIATION OF SOFT-TISSUE SARCOMAS

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Between 1978 and 1985, 221 patients with soft-tissue sarcomas were irradiated with neutrons or a neutron boost at the University Hospital in Essen (14 MeV d-Be). Patients with a minimum follow-up period of 1 year are analysed in this report. The dose and fractionation regimen followed the critera of the EORTC high LET particle therapy group and has been described elsewhere. Fifteen patients had T1 tumours, 100 T2 and 106 T3 tumours. Fifty-four tumours were scored G1, 107 G2 and 60 G3. One hundred and nine patients were irradiated with neutrons and 112 with a neutron boost after previous photon or electron irradiation with 40 Gy. Local control at last review was 100% for T1 tumours, 96% for T2 tumours and 69% for T3 tumours. The actuarial tumour-free survival rate of all patients at 5.5 years is 46.2%. For patients with T1 tumours it is 62.6%, T2 tumours 71.5% and T3 tumours 28.7% ($p = 0.016$). The difference between T1 and T2 tumours is caused by four metastatic deaths in the group of T1 tumours. Ninety per cent of recurrences as well as metastases occurred within 2 years after treatment. The survival rate for G1 tumours is 73.3%, G2 tumours 47.7% ($p = 0.035$) and G3 tumours 22.4% ($p = 0.024$). The type of resection also influences survival. It is 86.6% for microscopic complete resection, 65.6% for microscopic incomplete resection ($p = 0.042$) and 25.5% for macroscopic tumour residual ($p = 0.003$). A functional limb was preserved in 95% of patients with peripheral tumours. The complication rate is 25% in the neutron group and less than 10% in the neutron-boost group. These results suggest that post-operative neutron or neutron-boost therapy yields better local control rates than conventional irradiation in T2/T3, G1/G2 peripheral soft-tissue sarcomas.

NEUTRON THERAPY OF SPINAL SPONGIOBLASTOMA AND EPENDYMOMA. AN INTERIM ANALYSIS OF 10 CASES

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Between 1980 and 1985, seven patients with spinal spongioblastomas and three patients with Grade I ependymomas were irradiated with neutrons at the University Hospital in Essen ($d\ (14) + Be$). The mean follow-up period is 22 months with a range of 2–62 months. All patients had gross residual tumour after laminectomy. The neutron dose at the target volume varied between 7.4 Gy and 10.4 Gy (total dose, γ proportion $\sim 4\%$) delivered in eight to 13 fractions, three to four fractions per week. All patients suffered from serious neurological symptoms ranging from headache and paraplegia to complete bladder and rectal dysfunction. Five patients showed regression of their symptoms, which was complete in two and partial in three cases. Four patients showed no change in symptoms after neutron treatment. Progressive deterioration and death after 14.5 months was observed in one case with an epidural spongioblastoma. One girl developed a pronounced scoliosis requiring surgical correction 4 years after treatment. This complication may partly be attributed to neutron irradiation. To our knowledge, similar results have not been reported with conventional irradiation.

RESULTS OF NEUTRON THERAPY OF SOFT-TISSUE SARCOMAS, PROSTATE AND CERVICAL CARCINOMAS AT THE UCL-CLINIQUES ST-LUC, BRUXELLES

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At the UCL cyclotron of Louvain-la-Neuve, up to December 1981, neutron therapy was performed with neutrons produced by bombarding a beryllium target with 50 MeV deuterons; from 1982 neutrons have been produced using 65 MeV protons (additional filter 2 cm polythene).

From March 1978 to August 1985, 80 patients with soft-tissue sarcomas were treated. The tumours were located in the limbs (34), girdle, shoulder and trunk (20) and head and neck (four). In a first group of 26 patients, gross tumours were present: large, inoperable, incompletely resected or recurrent tumours. Some of the patients refused amputation. Persisting local control was obtained in six out of 26 patients. A second group of 32 patients with only "subclinical" disease was treated after "radical" surgery. Local recurrence was observed in two out of 32 patients. For both groups, 12 complications in 58 cases (21%) were observed. The minimum follow-up was 6 months. A total dose of 23.20 Gy (p(65)+Be neutrons) is currently given in 20 fractions over 6.5 weeks.

For locally advanced uterine cervical tumours, the RTOG protocol was followed. From November 1979 to December 1985, 46 patients were randomised between mixed-schedule (25) and photon (21) irradiations. Survival at 3 years was eight out of 13 after mixed-schedule and six out of 10 after photon irradiation. The corresponding recurrence rates were three out of 13 and three out of 10, respectively.

Locally extended prostatic adenocarcinomas, Stage C, are currently treated with mixed-schedule irradiation. The RTOG protocol is followed, but with three neutron and two photon fractions per week. From October 1979 to December 1985, 36 patients were treated (15 with tumour present, and 21 after TURP). At 3 years, the local control rate was 13 out of 17 (76.5%) and the survival 12 out of 17 (70.5%). At 4 years, the local control rate was five out of six and the survival six out of six. Only one complication (after TURP) was observed

THE NEUTRON THERAPY PROGRAMME AT THE DOUGLAS CYCLOTRON CENTRE, CLATTERBRIDGE HOSPITAL

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The Clatterbridge cyclotron produces high-energy neutrons (62.5 MeV protons on Be) with depth-dose characteristics similar to those of a beam of 6 MV linear-accelerator X rays. The neutron treatment plans produced are therefore comparable with those for megavoltage X rays, particularly in the treatment of deep-seated pelvic tumours. This has helped to overcome many of the treatment planning problems associated with the use of lower-energy neutrons.

Clinical studies were started in February 1986. The tumour types and sites initially being studied are locally advanced squamous-cell carcinoma in the head and neck and locally advanced squamous-cell carcinoma of the cervix, transitional-cell carcinoma of the bladder and adenocarcinoma of the rectum and prostate. All patients eligible for entry into the studies are randomised to receive neutron or conventional photon radiotherapy. The patients give informed written consent before being randomised. An important eligibility criterion is that comparable neutron and photon treatment plans must be produced.

In the head and neck study the prescribed minimum target dose is 20.4 Gy (neutrons+γ) given in 12 fractions over 28 days treating three times per week. Collaboration with the Department of Radiation Oncology, University of Washington Hospital, Seattle, USA, is soon to start in a Phase III study of high-energy neutrons versus photons in advanced squamous-cell carcinoma of the head and neck. In the investigation of fast-neutron therapy in advanced pelvic cancer a minimum target dose of 19.2 Gy (n+γ) is given in 12 fractions over 28 days. The treatment is given to an initial large volume (14.4 Gy in nine fractions) and where feasible to a reduced volume for the final 4.8 Gy in three fractions.

Computed tomography is used at all stages in treatment planning and target volume isodosing procedures. Precise treatment planning is only one of the important factors involved in assessing the role of high-energy neutrons in the management of locally advanced malignancy (Errington, 1986).

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Book reviews

Hand-held and Automated Breast Ultrasound. By L. W Bassett, R. H Gold and C Kimme-Smith, pp xi+204, 1986 (John Wiley, Chichester), £45.50.
ISBN 0–943432537

Although the preface indicates that this book is for those practising breast ultrasound and for those about to start using the technique, my impression is that the book is aimed principally at the latter group. After a brief historical introduction, there are chapters on the physics and instrumentation which are clearly written and readily understandable, and which would be particularly valuable for those starting in breast ultrasound.

This chapter on benign conditions focuses principally on benign masses, and both in this chapter and in the chapter on malignant conditions I would have welcomed a greater number of illustrations to show the possible range and overlap between benign and malignant tumours At this point, I have to say that I found the small number of illustrations which were produced in the black echo/white background format difficult to interpret—I am sure most workers would prefer the alternative white echo/black background format. The illustrations in general illustrated the points made in the text. The penultimate chapter on pitfalls was a useful summary, but I would have preferred the final chapter to have been devoted to a wider illustration of diseases, rather than the quiz format.

In general, this book is good value for money, it is up to date and should prove very useful to those with little experience of breast ultrasound for whom it is strongly recommended.

P B. GUYER

Physical Principles of Medical Ultrasonics. Ed. by C. R Hill, pp. 495, 1986 (Ellis Horwood, Chichester), £45.00.
ISBN 0–853122083

It would not be an exaggeration to say that this substantial and well written book marks the coming of age of the science of medical ultrasound. The extensive clinical contributions of diagnostic ultrasound during the past couple of decades have given rise to many other useful texts, most dealing with clinical applications and engineering design. Perhaps surprisingly, however, many advances have occurred without a full and well documented understanding of the underlying physical principles, which have been only slowly revealed by the work of a few international groups. This book, edited by Professor C R. Hill, fills a recognised gap in the bibliography of medical ultrasound by bringing together in one formal text current knowledge of the physical science upon which therapeutic and investigative ultrasound are based, drawn very much from the substantial experience and perspectives of the Institute of Cancer Research. Several chapters have been contributed by authors from this Institute. For instance Dr Bamber's contributions on attenuation, absorption and speed of sound are particularly valuable and rely strongly upon his personal contributions to the measurements of these quantities. Three well referenced chapters by Dr Gail ter Haar very thoroughly cover the biophysical implications of ultrasound and its use for therapeutic applications. The formal theoretical basis of ultrasonic wave propagation presented by Dr Miller is significantly more complete than in any other comparable text and would act as a firm basis for any further theoretical developments. Similarly, the mathematical basis of scattering is discussed adequately by Dr Dickinson in a chapter which could form a firm theoretical platform for anyone contemplating carrying out further work in this area. Elsewhere in the volume other topics—Doppler theory, ultrasonic field theory, tissue characterisation (telehistology)—are dealt with in a similarly careful and complete way Sensibly omitted is any detailed description either of the sophisticated technology required to generate modern ultrasound images or of their clinical use. These topics are very well covered elsewhere, and their omission in no way detracts from Professor Hill's book. Generally the illustrations support the text well although it is here where some criticism may be made, there being some unevenness of style and quality between chapters contributed by different authors. In addition, the quality of reproduction of the few ultrasonic images shown would not have been tolerated in a clinical ultrasound text. The references are largely complete to 1985 and misprints in the text are minor.

For anyone wishing to obtain a definitive text dealing with the scientific basis of medical ultrasound, the purchase of this book is essential. It is certain to become a reference book for any course teaching the physics of medical ultrasound at anything more than a superficial level. Finally, it will provide the necessary groundwork for any scientist wishing to contribute further in this still expanding field of endeavour.

F. A. DUCK

NMR in Biology and Medicine Ed by S Chien and C Ho, pp. 275, 1986 (Raven Press, New York), $62 00
ISBN 0–88167–231–9

This book records the proceedings of an international symposium on nuclear magnetic resonance (NMR) in biology and medicine held in 1984 to introduce newer concepts in NMR to the Republic of China in Taiwan There were 13 invited speakers from Europe and the USA, each of whom contributed a chapter

Nuclear magnetic resonance imaging of the cardiovascular system and musculo-skeletal system is well reviewed. The imaging section is completed by a brief introduction to spectroscopic imaging and NMR microscopy. *In-vivo* spectroscopy is covered in three chapters all concentrating on the role of ^{31}P NMR in muscle metabolism. This section demands a little background of biochemical and spectroscopic knowledge, although the chapter by Radda and Chien (from Oxford) is very readable.

The remainder of the book (131 pages) is devoted to the biological applications of NMR and, in particular, the study of cell membranes and molecular structure This section is more specific and more detailed. It can be of little interest to those without the appropriate biological background and those familiar with the field will find little new here.

The book is well produced, although there are a few spelling errors. Tables are readable, but NMR images are less well reproduced and some appear dated. The book succeeds in its modest aim of recording what was no doubt a stimulating meeting. However, the book attempts to cover far too much ground to succeed as an NMR text Those interested in NMR will find better value for money and the book cannot be recommended for either library or individual purchase

GRAHAM R. CHERRYMAN

BIR North of England Branch: 1986 Autumn Meeting

The 111th meeting of the North of England Branch of the BIR was held at the Bolton Medical Institute, on Saturday, October 18, 1986 The following papers were presented at the meeting

The President of the Institute, Professor R. J Berry, attended the meeting and encouraged closer links between the Branch and the Institute headquarters. In the course of the day he had occasion to admire the badge of office of the Chairman, which was given to the Branch in 1982 by the then chairman, Dr F. B Wright

Internal jugular vein thrombosis: a rare presentation of malignancy

B Carrington, Booth Hall Children's Hospital, Manchester

The aetiology and diagnostic features of internal jugular vein thrombosis is discussed with reference to two patients in whom it was a manifestation of distant malignant disease. Computed tomography was shown to be of value in its diagnosis and in the assessment of the primary malignancy

The skull radiograph in head injury: a critical appraisal including its financial implications

J. A. Clarke, Manchester Royal Infirmary

It has been shown that a fracture is present in only 2% of skull radiographs performed in the accident and emergency department 6 000 000 skull radiographs are requested annually at an estimated annual cost of £6 6 million A study by the Royal College of Radiologists (RCR) has shown that many are unnecessary and therefore guidelines were drawn up to select those patients with a head injury who should be radiographed (RCR, 1983) Using such guidelines it is possible to reduce the number of skull radiographs by 50% without adversely affecting patient management, thereby achieving a substantial financial saving (Fowkes et al, 1984)

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RCR, 1983. Patient selection for skull radiography in uncomplicated head injury *Lancet i*, 115–118.

Coating and filling on barium enema

Anthony Maxwell, Hope Hospital, Salford

Mucosal coating of the colon in double-contrast barium enema is often less than ideal, especially in the right side of the colon A study was performed comparing mucosal coating using two different concentrations of Polibar barium (E-Z-EM Co. Inc) in order to assess whether the use of a more dense suspension results in improved coating. Thirty-six examinations were performed with the standard 67% barium (500 ml of water per 400 g bag of barium) and 33 examinations with 80% barium (400 ml water per 400 g barium) using a standardised technique including the routine use of smooth-muscle relaxants Mucosal coating in each of four segments of the bowel was assessed independently by two observers using a standard scoring system. In addition, terminal ileal and caecal filling and distension were studied before and after evacuation

(i) There was no significant difference in mucosal coating properties between the two barium concentrations; (ii) coating decreased significantly moving proximally from sigmoid to caecum, (iii) there was no significant age effect; and (iv) there were significant observer differences. Thus, there is no advantage to be gained by the use of 80% Polibar rather than the standard 67% suspension, especially as the 80% suspension is more viscous. The terminal ileum was filled in approximately two-thirds of patients prior to evacuation, but only approximately 20% show better distension of the terminal ileum on the post-evacuation film, and of the remaining one-third only approximately 10% show terminal ileal filling after evacuation Only approximately 20% of patients show improved caecal distension after evacuation. Thus, the post-evacuation film should not be relied upon to demonstrate a well distended terminal ileum or caecum if these have not been seen prior to evacuation

Bile-duct dimension in obstructive jaundice

Andrew Chippindale, University of Manchester Medical School

In order to assess whether the gall-bladder can protect the bile ducts from dilatation following bile-duct obstruction, corrected bile-duct diameters were recorded in 98 patients undergoing endoscopic retrograde cholangiography for obstructive jaundice at Withington Hospital, South Manchester. Comparison was then made between those with and those without gallbladders, using analysis of variance (significance set at the 5% level). Data were also analysed with respect to the nature of the underlying pathology, in order to see if those with gallstone obstruction experienced a different degree of bile-duct dilatation from those with neoplasm.

Bile-duct diameters were larger in female patients (significant at the 5% level) and in the elderly. There was, however, no difference in bile-duct diameters between those with and those without gallbladders The nature of the underlying obstructive pathology was not found to affect the degree of bile-duct dilatation

Preparing a paper for publication

J. T. Patton, Manchester Royal Infirmary

The reasons for writing a paper are discussed along with the consequent need to write down these reasons so that, as writing proceeds, the writer does not find he is digressing too far from his or her original aim, there being always a temptation, as in a lecture, to try and say too much.

The medical writer is helped by the framework of: summary (or abstract), introduction, method, results and discussion, which has now become the standard form of most publications

The physical method of putting thoughts down on paper (or tape) are personal but after the first draft stage the enormous advantage of a word processor in saving secretarial time is emphasised.

It is recommended that before submitting a paper it is read by a colleague in a different field in order to avoid the assumptions made by somebody too familiar with it. The title should be chosen after the paper is completed and ideally would be short and calculated to attract a reader.

With regard to literary style, although it is important to avoid clichés and gross grammatical solecism, it is felt that the aspirant author should worry more about the contents and leave the English to the editor.

In book reviews it is important to try and tell the reader honestly if a book is worth buying but, although forthright criticism of a book is perfectly in order, it is important not to be over facetious or to try and score points. A book review is primarily a measure of a book, not the wit of the reviewer. It is only rarely one can justify the devastating but nevertheless constructive comment by Richard Asher. "Professor Wintrobe, dealing with haematology, certainly knows what he is talking about; but I am not sure that his readers will".

Three-dimensional computed tomography

J Gillespie, Department of Diagnostic Radiology, University of Manchester Medical School

Superimposition of bony structures and problems involved in the assimilation of information from multiple tomographic or computed tomography (CT) slices can make it difficult for the observer to conceptualise the third dimension. This is a particular problem in areas of complex anatomy such as the facial skeleton or pelvis Computer software to facilitate the production of three-dimensional (3D) reformations from a series of conventional CT sections has been employed in a number of centres in attempts to overcome this problem.

Over a 2-year period 3D reforming of CT data derived from an IGE 8800 or 9800 CT scanner has been performed in the Department of Diagnostic Radiology, University of Manchester, using the software packages 3D83 and 3D98, respectively. Patients presenting with congenital, traumatic and neoplastic abnormalities of the axial skeleton and brain formed the main areas of clinical study. Three-dimensional reformating has been found to be most useful in: severe congenital and traumatic injuries, particularly involving the face, extensive areas of skull base erosion; and for displaying the vascular relations of large enhancing intracranial tumours. The 3D image format is ideally suited to the assimilation and communication of complex spacial information. Examples of the use of 3D imaging in the clinical management of a variety of abnormalities are presented.

Press releases

Proceedings of Varian Accelerator Users Meeting published

The Varian Users Meeting *Proceedings*, a 110-page publication containing all the scientific and technical papers presented at the 11th Varian Users Meeting, has been published by Varian Associates, Inc. The papers, delivered during the three-day meeting held in Florida, cover a wide range of subjects dealing with radiotherapy treatment techniques, research results, and new equipment accessories developed to enhance radiotherapy procedures with medical accelerators.

The special emphasis of the meeting was "Radiotherapy Toward The Year 2000" During four technical sessions, practitioners presented their views on new treatment modalities, new treatment techniques, and on the anticipated evolution in the roles of radiotherapy professionals Speakers also stated their views on the direction in which radiotherapy is now moving.

Copies of the *Proceedings* are available free of charge. Requests should be addressed to Varian Associates, Inc, Radiation Division, 611 Hansen Way, Box MGM, Attn Users Proceedings Editor, Palo Alto, CA 94303, USA

British Antarctic Survey ship transmits radiographs to Aberdeen

The British Antarctic Survey ship, The Bransfield, left the UK last November on its annual tour of the South Antarctic, equipped with slow-scan TV equipment loaned by Colorado Video Inc. to enable TV pictures to be transmitted over the telephone in an experiment designed by Professor Nelson-Norman of the Centre for Offshore Health and Professor Gillanders, Head of Radiology, Aberdeen Royal Infirmary, TV pictures of medical radiographs were transmitted, via the ship's satellite communications system, back to Aberdeen for diagnosis by radiological experts

It was intended to demonstrate the feasibility of sending TV pictures over a wide geographical area, including South America, The Falklands and the Antarctic Survey bases, and to assist the young medical officers of the survey by providing the expertise of the specialists back home for radiographs which are difficult to interpret.

For further information on telediagnosis contact Colorado Video's UK representative: Brian Reece Scientific Instruments, The Chantry, West Mills, Newbury, Berkshire RG14 5HG (Tel. 0635-32827).

Hard-copy prints from video signal

The new Model P70B Video Copy Processor from Brian Reece Scientific Instruments provides high-resolution, near photographic quality, hard-copy prints from a standard composite video signal, as could be provided from a video camera, monitor display or video cassette recorder. High-performance thermal heads give A4-size prints in about 20 seconds. The unit incorporates its own video-frame store with a resolution of 640 pixels by 289 lines Inputs include composite video (625 or 525 line), RGB/TTL, Centronics and Teletext Other features include reversible print direction, negative print capability, remote control and multiple copying. For further details or a demonstration please contact: Brian Reece Scientific Instruments, The Chantry, West Mills, Newbury, Berkshire RG14 5HG (Tel. 0635-32827)

Offer from Adam Hilger

Adam Hilger Publishers, Bristol, are making a special offer to BIR members 25% off the price of many of their current medical physics books. Watch out for a loose insertion from the publishers in a forthcoming issue of the *BJR*, giving details of this valuable offer.

New radiology index

The new 1982–85 *Index of European Radiological Journals (IERJ)* is a 400-page volume, published in English, which includes all the references of 29 European journals devoted to diagnostic imaging, therapeutic radiology and nuclear medicine. One of the goals of the *IERJ* is to make American and European authors aware of the available European references. The *IERJ* receives the support of the European Association of Radiology. It is available for reference in the Library.

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Burrows, E. H.: Pioneers and early years. A history of British radiology. 1986

Heilmann, H. P. (Ed.): Radiation therapy of malignant tumours, Parts 4–5 1984–85 (Encyclopedia of medical radiology. 19)

Rosenberger, A. & Boijsen, E (Eds): Radiology in war. Acta Radiologica, Suppl 367. 1986

Current journals held in the BIR Library

Acta Radiologica—Diagnosis
Acta Radiologica—Oncology
American Journal of Neuroradiology
American Journal of Roentgenology
Annales de Radiologie
Annals of the ICRP
Applied Health Physics, Abstracts and Notes
Applied Radiation and Isotopes
Astro Newsletter
Australasian Radiology
BMUS Bulletin
British Journal of Cancer
British Journal of Radiology
British Medical Bulletin
British Medical Journal
British Society of Dental and Maxillofacial Radiology Newsletter
BSI News
Cancer
Cancer Research
Cancer Research Campaign Annual Report
Cancer Treatment Reviews
Cardiovascular and Interventional Radiology
Cell and Tissue Kinetics
Chinese Journal of Nuclear Medicine
Chinese Journal of Radiology
Clinical Nuclear Medicine
(Clinical Oncology cont as European Journal of Surgical Oncology)
Clinical Physics and Physiological Measurements
Clinical Radiology
Computerized Radiology
Critical Reviews in Diagnostic Imaging
Current Contents (Life Sciences)
Current Opinion in Cardiology
Current Opinion in Gastroenterology
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Diagnostic Imaging (USA)
European Journal of Cancer and Clinical Oncology
European Journal of Nuclear Medicine
European Journal of Radiology
European Journal of Surgical Oncology
Excerpta Medica 14 Radiology
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ISRRT Newsletter
Indian Journal of Radiology
International Agency for Research on Cancer Annual Report
International Atomic Energy Agency Bulletin
International Journal of Hyperthermia
International Journal of Radiation Biology
International Journal of Radiation Oncology, Biology, Physics
Investigative Radiology
Japanese Journal of Nuclear Medicine
Journal Belge de Radiologie
Journal de Radiologie (France)
Journal Européen de Radiothérapie
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Journal of Clinical Ultrasound
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Journal of Computer Assisted Tomography
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Journal of The National Cancer Institute
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Radiologia Medica (Italy)
Radiologic Clinics of North America
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Seminars in Nuclear Medicine
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Skeletal Radiology
Strahlentherapie
Ultrasonic Imaging
Ultrasonics
Ultrasound in Medicine and Biology
Urologic Radiology
World Health
Yearbook of Diagnostic Radiology

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary, Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Annual General Meeting
May 14, 1987 at 4 30 p m

Imaging in Radiotherapy
May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced
Topics are expected to include integrated treatment planning, special imaging techniques, radiotherapy portal imaging, three-dimensional imaging and simulator CT.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione
May 20, 1987
Royal Naval College, Greenwich

Advance Notice

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1–3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and includes:
The BIR Mackenzie Davidson Memorial Lecture, by Professor M. J. Peckham, "The clinical biology of testicular germ cell tumours"
The BIR Mayneord Lecture (sponsored by 3M UK plc), by Miss Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"
The RCR George Simon Lecture, by Sir John Batten, "Radiology and cystic fibrosis"
The BIR Presidential Address, by Professor R J Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

For further information and registration forms please apply to the Assistant Secretary Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085).

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge. any additional information will be charged at £1 75 per printed line, per insertion. Please contact the Managing Editor.

69th Annual Meeting of the American Radium Society
April 6–10, 1987
The Portman Inter-Continental, London
Further details: Office of the Secretariat, American Radium Society, 925 Chestnut Street, Philadelphia, PA 19107, USA.

Thoracic Imaging: 1987
April 9–11, 1987
Monterey, USA
Further details. Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Avenue, San Francisco, CA 94143-0628, USA (Tel. 415-476 5731).

Obstetric, Gynecologic and Abdominal Sonography: Update 1987
April 10–12, 1987
San Francisco, USA
Further details. Radiology Postgraduate Education, University of California, Room C324, Third & Parnassus Avenue, San Francisco, CA 94143-0628, USA (Tel 415-476 5731).

Cardiovascular and Interventional Radiology and New Imaging Modalities
May 25–29, 1987
Sardinia, Italy
Joint meeting of the European and American Societies of Cardiovascular and Interventional Radiology with participation of the Japanese Society.

Further details. Prof. P. Rossi, Instituto di Radiologia della Universita, Policlinico Umberto 1, I-00161, Italy (Tel. 01039-6495 5602).

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details: Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123–7° DTo, 1000 Lisboa, Portugal, (Tel: 77–05 30, Telex 62074 SPRMN P).

34th Annual Meeting of the Society of Nuclear Medicine
June 2–5, 1987
Toronto, Canada
Further details: Society of Nuclear Medicine, Education & Meetings Department, 136 Madison Avenue, New York, NY 10016, USA (Tel 212-889 0717)

The Cambridge Meeting on Frontiers in Ultrasound
July 3–4, 1987
King's College, Cambridge
Further details: Dr John Tudor, Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

Chest Imaging Conference (CIC-87)
August 31–September 2, 1987
Madison, Wisconsin, USA
Further details. John R. Cameron, Department of Medical Physics, 1530 MSC, 1300 University Avenue, Madison, WI 53706, USA (Tel 608-262 2171).

3rd Annual Clinical Hyperthermia Symposium and Workshop
September 17–19, 1987
St Louis, Missouri, USA
Further details: Bahman Emami, M D., Symposium Chairman, Division of Radiation Oncology, Mallinckrodt Institute of Radiology, 4939 Audubon Avenue, Suite 5500, St Louis, Missouri 63110, USA (Tel. 314-362 8500)

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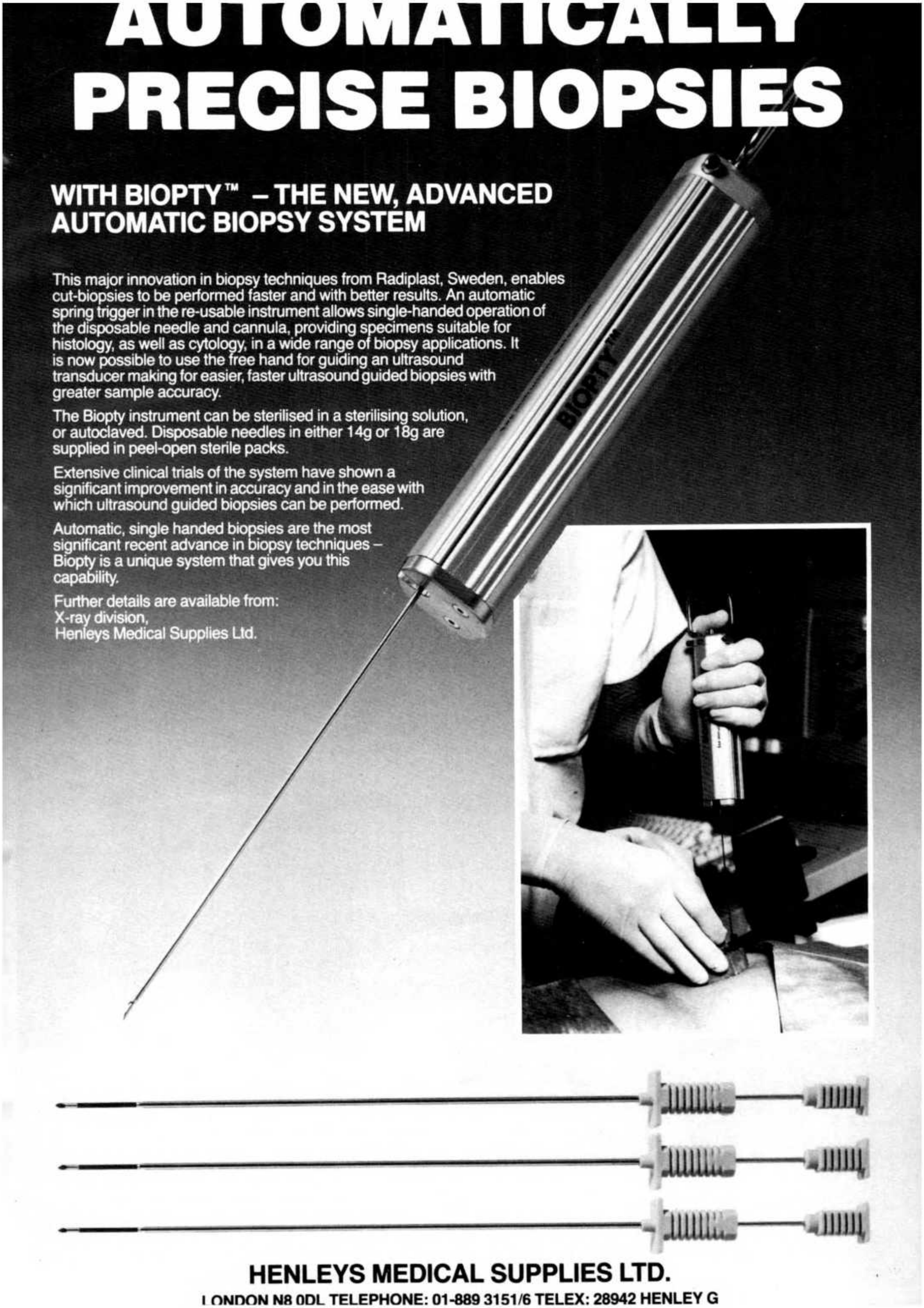

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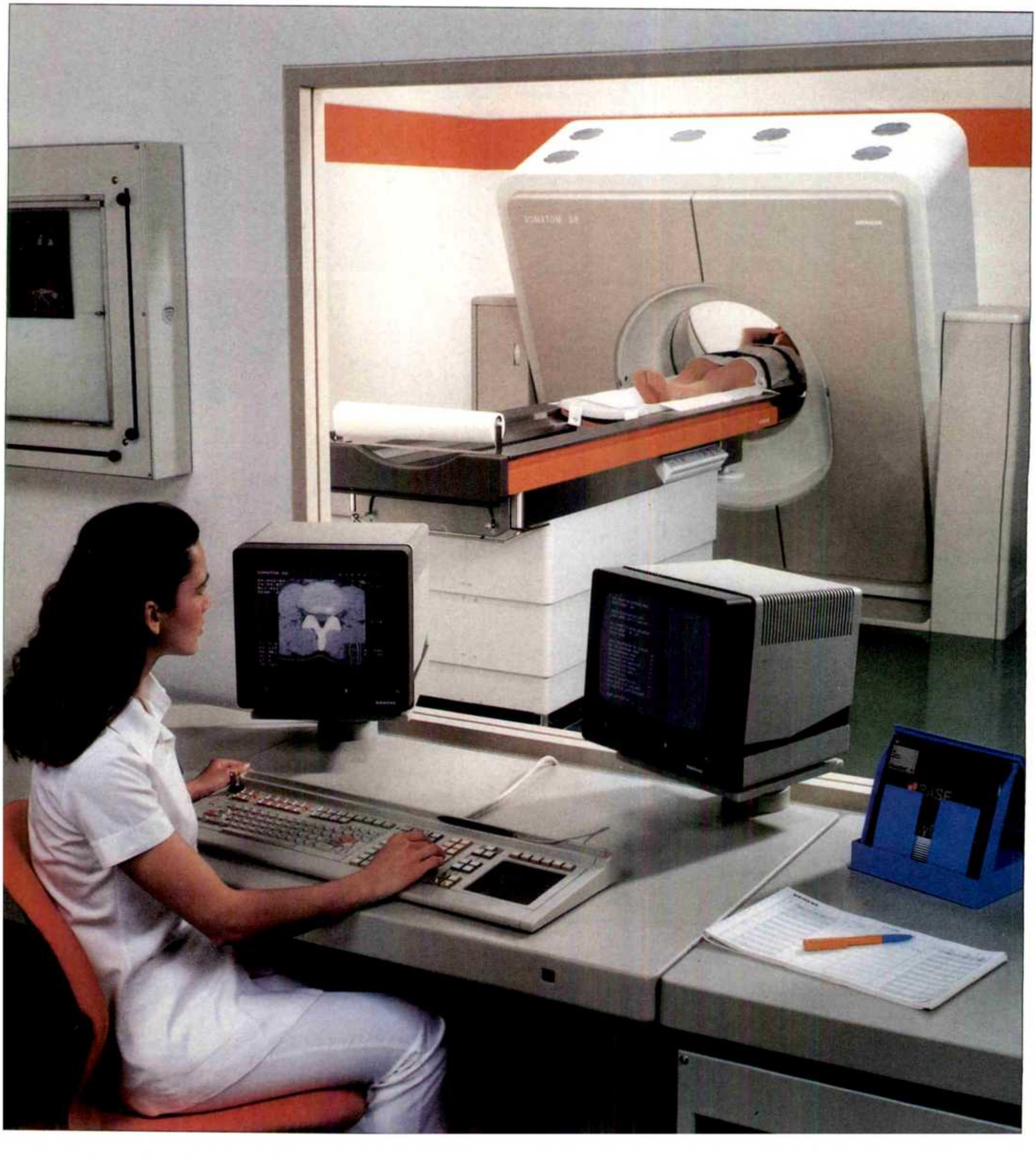

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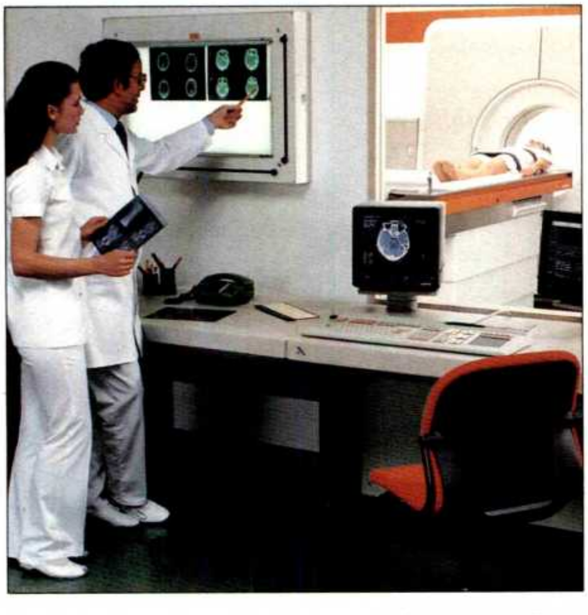

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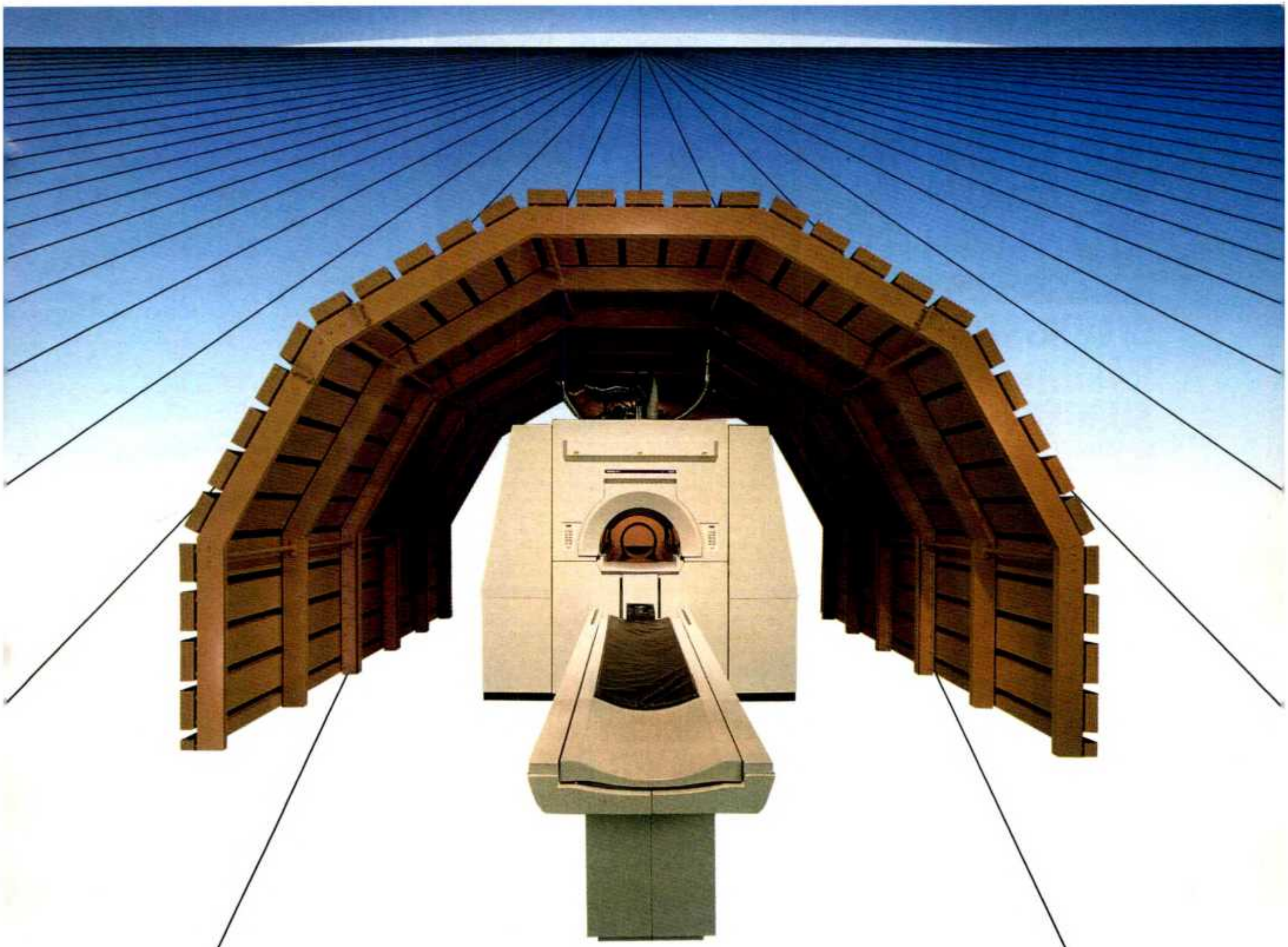

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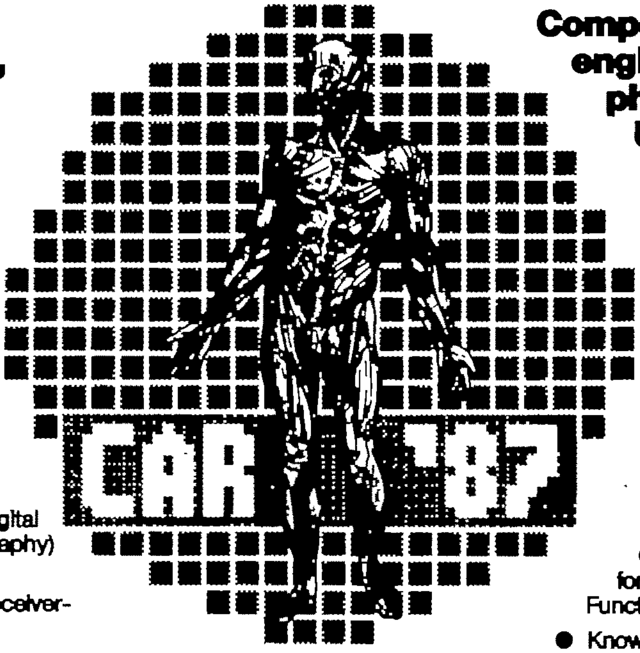

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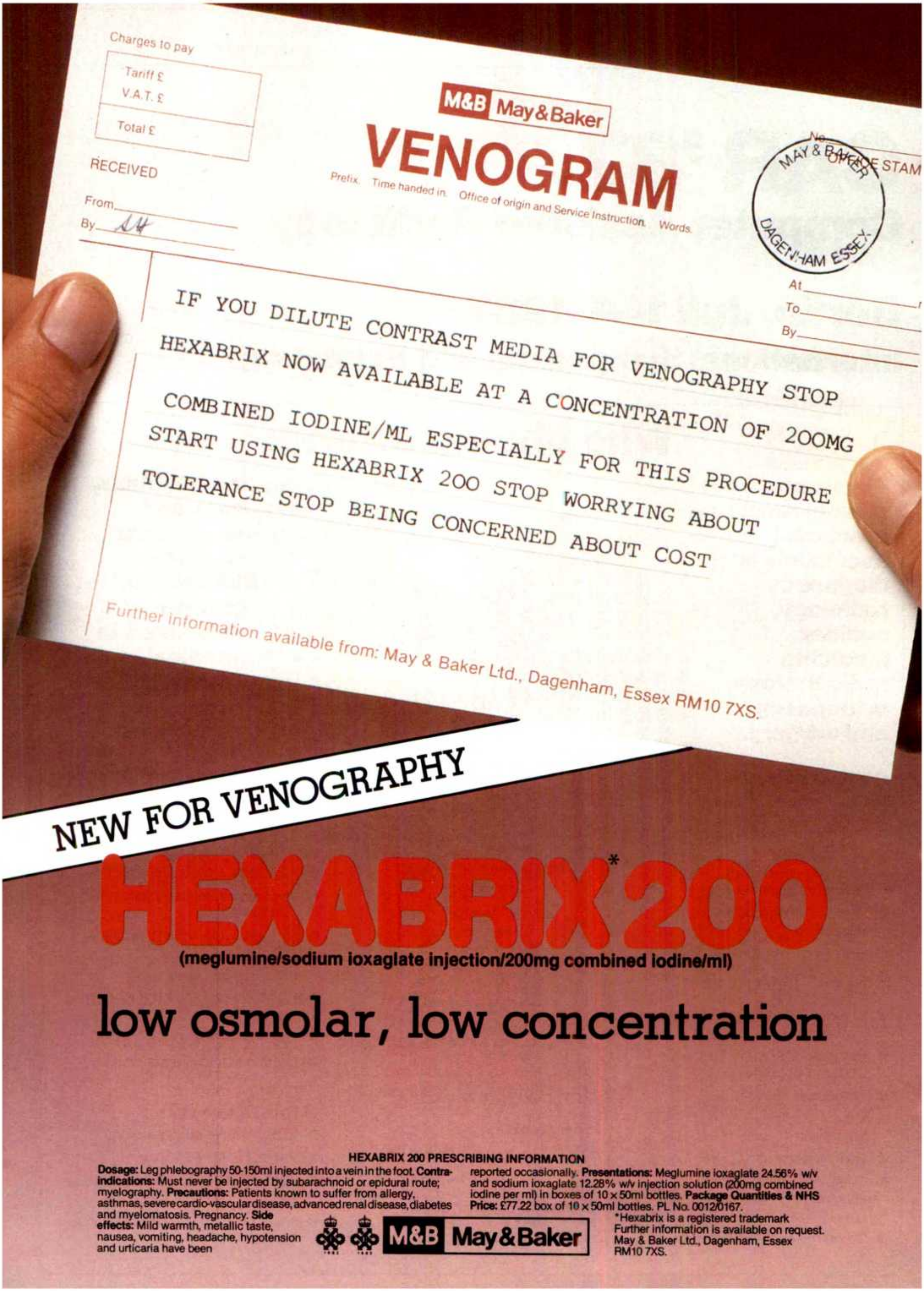Charges to pay
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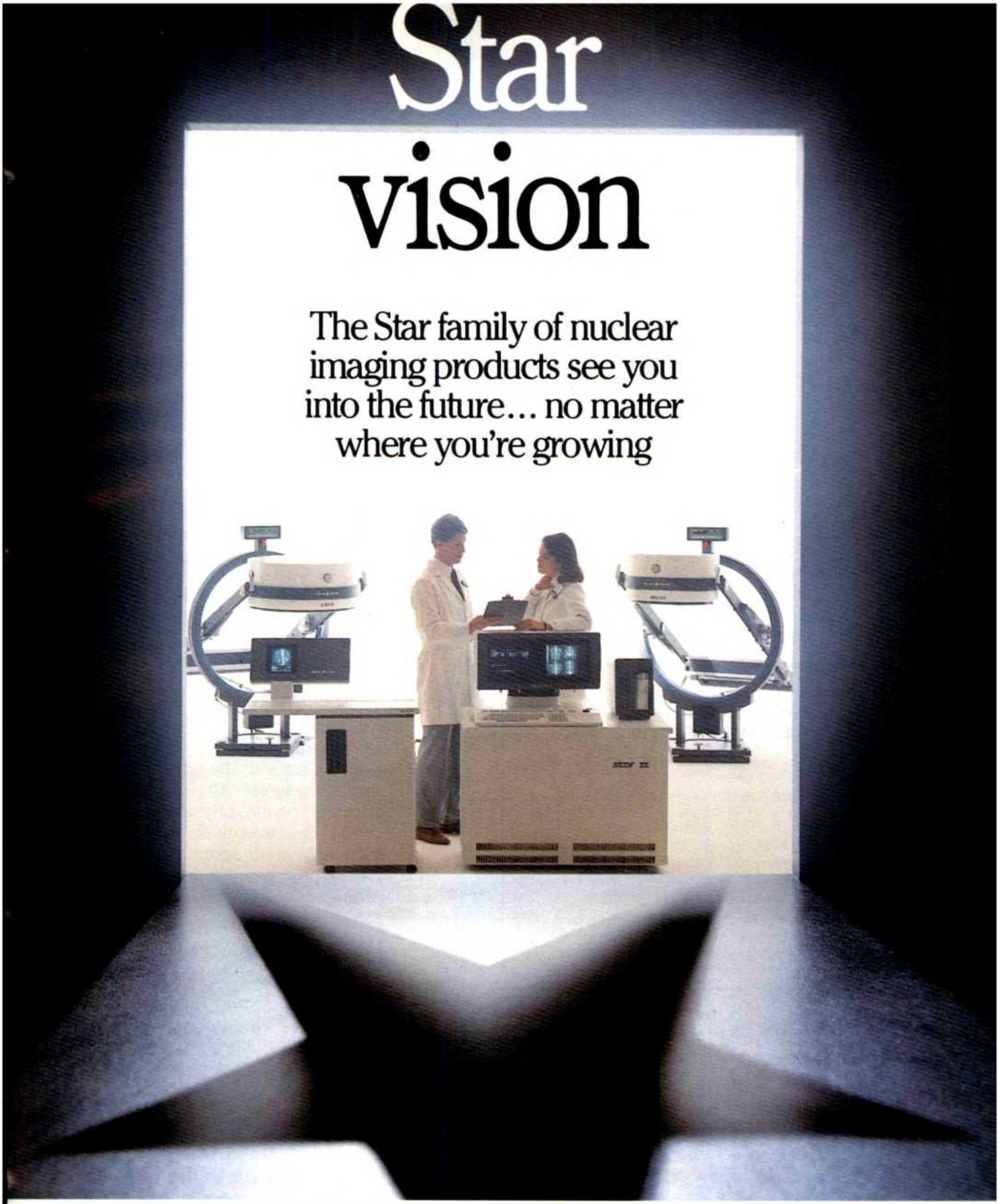
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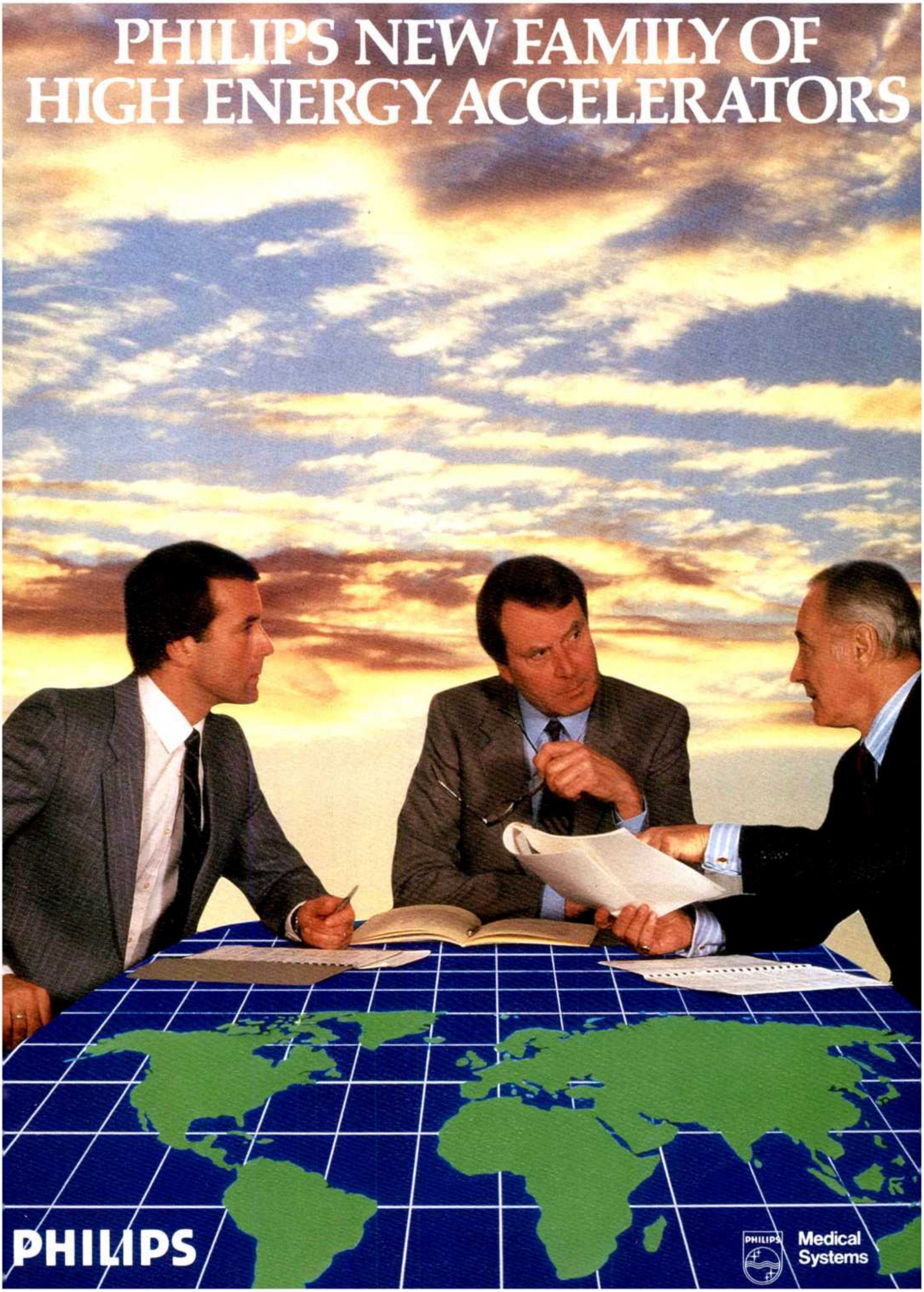

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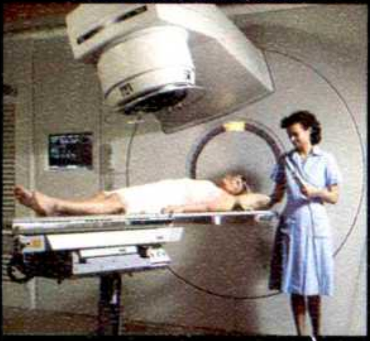

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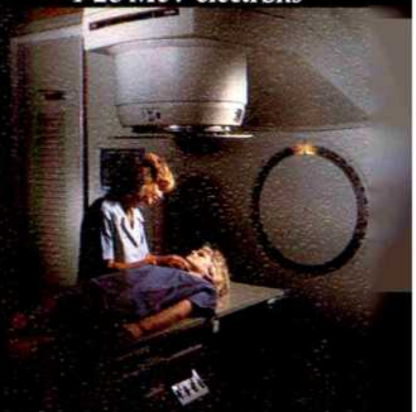

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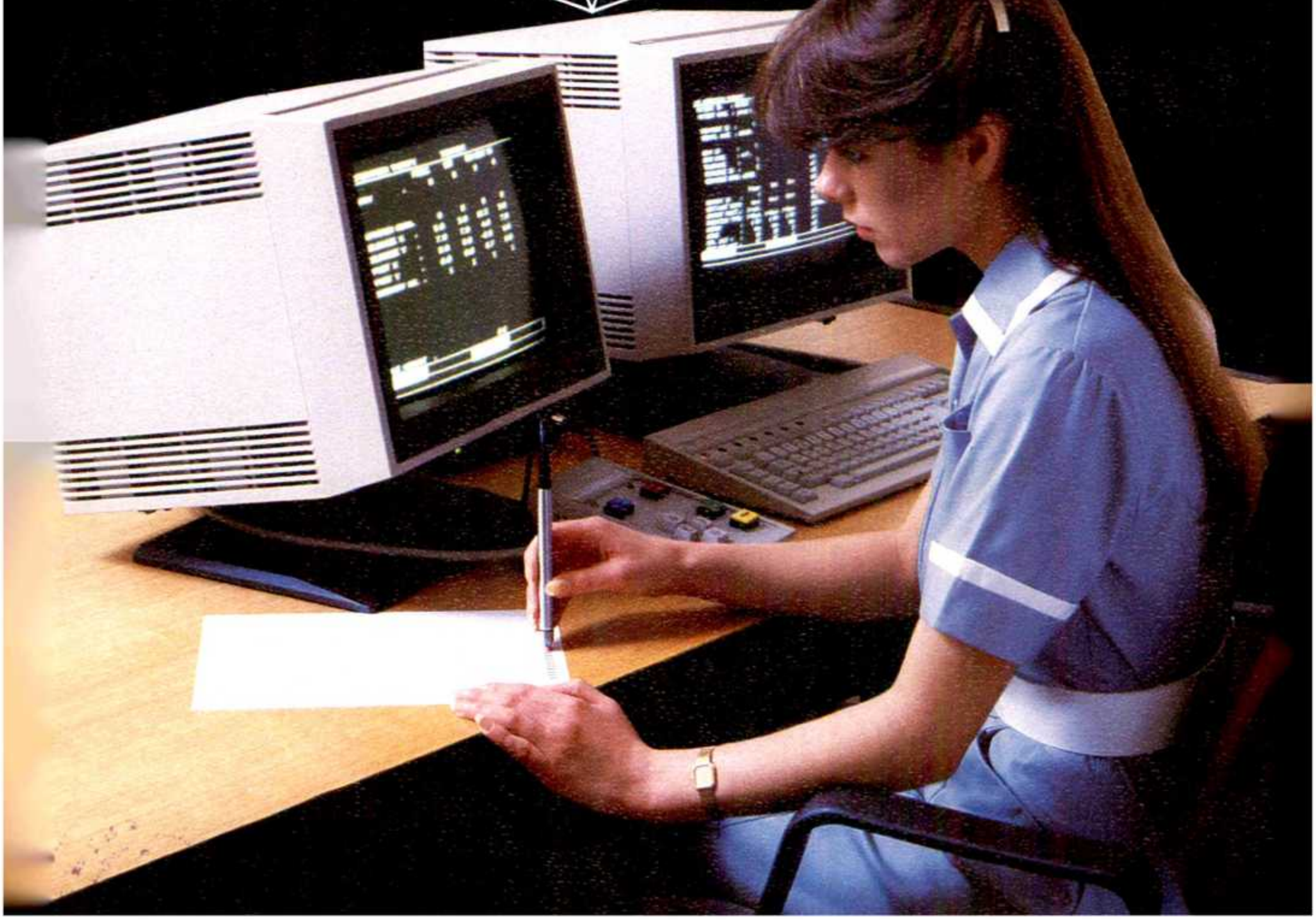

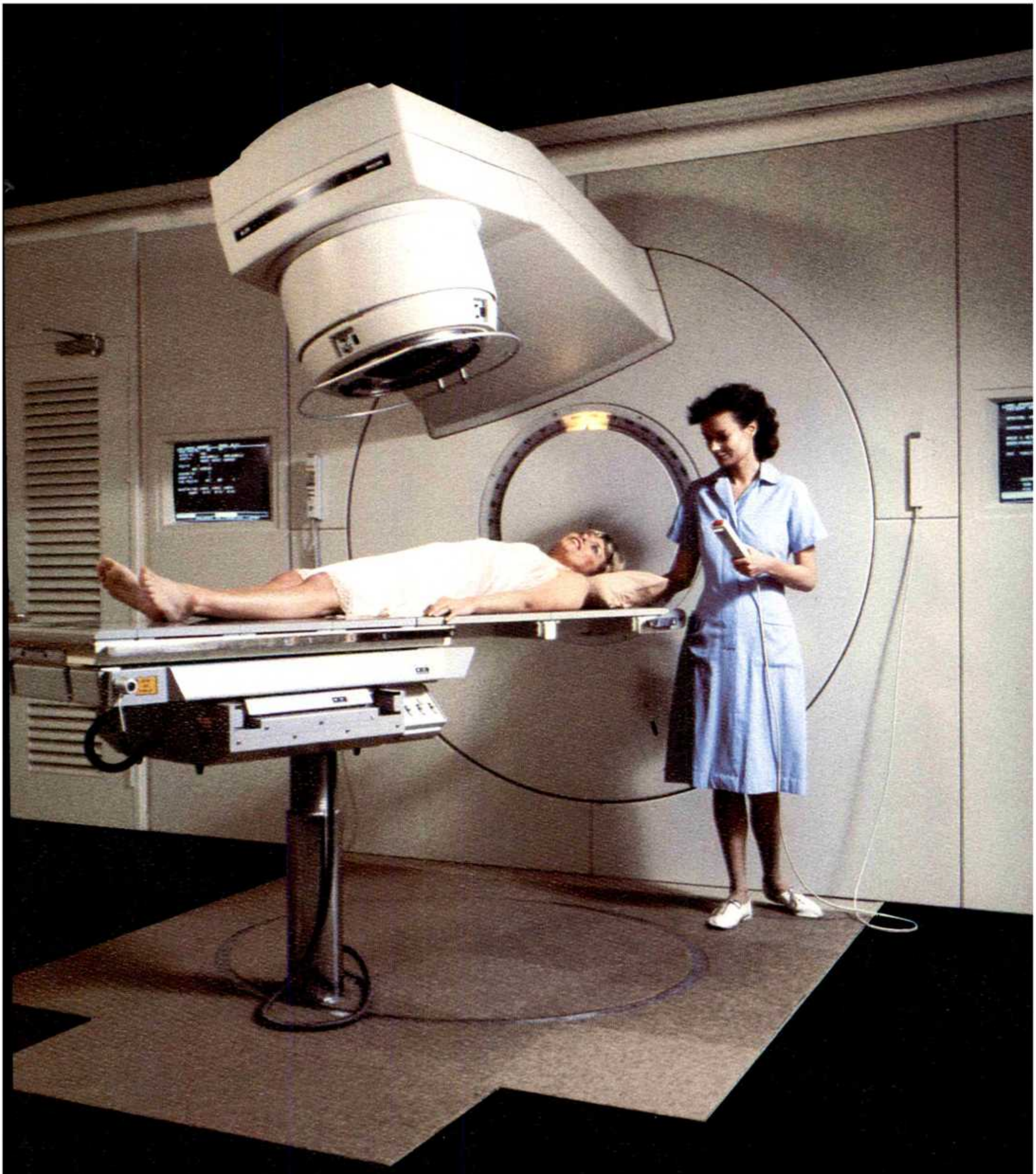

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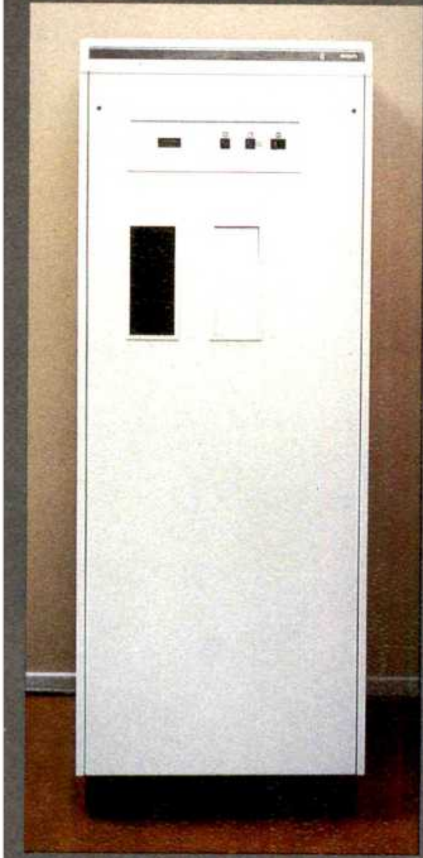

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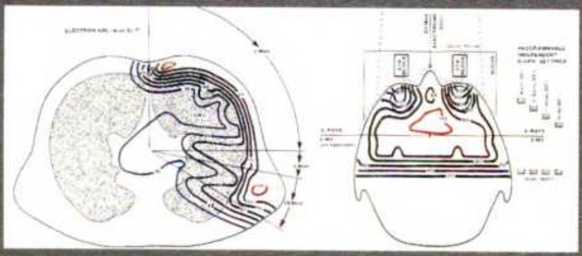

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Intravenous digital subtraction angiography in intracranial aneurysms

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ABSTRACT

Intravenous digital subtraction angiography was undertaken in 121 patients with known intracranial aneurysms. Its role in the management of these patients and its diagnostic accuracy have been assessed.

Intravenous digital subtraction angiography (DSA) is a simple and safe technique but lacks the resolution and selectivity necessary for the pre-operative assessment of intracranial aneurysms. Nevertheless, potentially valuable information can be obtained in the peri-operative period using intravenous DSA (Enzmann et al, 1982; Modic et al, 1981) and we describe our experience over 3 years at the Manchester Royal Infirmary involving 121 patients.

PATIENTS AND METHODS

Between January 1983 and December 1985, 121 patients with known intracranial aneurysm underwent intravenous DSA. A total of 132 studies were performed; in 85 patients these were performed in the post-operative period. Thirty-six patients had not undergone prior surgical treatment.

An International General Electric IGE LUA Fluoricon 3000 Digital Imaging System was used and the non-ionic contrast medium iohexol (Omnipaque 350, Nycomed UK Ltd) was administered via a short 16G cannula into an antecubital vein. All examinations were carried out in conscious patients and sedation was avoided as it prevented adequate patient co-operation.

RESULTS

Our indications for intravenous DSA in intracranial aneurysm are given in Table I, together with the number of patients studied and intravenous DSA examinations undertaken.

TABLE I

INDICATIONS FOR INTRAVENOUS DSA IN INTRACRANIAL ANEURYSM

Indications	No. of patients	No. of studies
Confirmation of CT diagnosis	6	6
Detection of arterial spasm	3	6
Assessment of aneurysm obliteration	47	53
Follow-up	65	67
Totals	121	132

Confirmation of a CT diagnosis

Occasionally computed tomography (CT) reveals the presence of clinically unsuspected aneurysms. There were six such cases in our series. Intravenous DSA, in common with other forms of angiography, may indicate true aneurysmal size, whereas CT will show any thrombosis within an aneurysm as well as the patent lumen.

Detection of arterial spasm

Three patients underwent six intravenous DSA studies specifically to detect spasm of the major intracerebral arteries. Repeated studies were required in order to monitor progress in some of the patients rather than because of inadequate initial examinations. Intravenous DSA proved adequate and reliable for this purpose. An incidental finding was evidence of arterial spasm from the intravenous DSA studies of several patients in the early post-operative period.

Assessment of aneurysm obliteration

Forty-seven patients underwent 53 intravenous DSA studies approximately 7 days after surgery. Comparison was made with intra-operative assessment of the adequacy of either the clipping or the wrapping of an aneurysm. Agreement was found in all but one instance. In the latter, access to a basilar artery aneurysm had proved difficult. The post-operative intravenous DSA

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TABLE II

LOCATIONS OF ANEURYSMS

Aneurysm types	Numbers
Posterior communicating artery	6
Anterior communicating artery	4
Middle cerebral artery	11
Basilar artery	2
Ophthalmic artery	1
Internal carotid artery	8
Total	32

revealed that the aneurysmal sac was incompletely clipped, whereas at operation it was judged to have been obliterated. This enabled the surgeon to re-operate successfully on that patient and occlude the aneurysm.

It is concluded that intravenous DSA is a reliable method of assessing the success or otherwise of surgery in the early post-operative period and that there was no prolongation of inpatient stay because of the angiography *per se*.

Follow-up

A total of 65 patients were examined in this category. Thirty-eight had previously undergone surgery involving either clipping or wrapping of an aneurysm or carotid artery ligation. Nine aneurysms were seen in the 36 patients who had undergone carotid ligation. Thirty-two aneurysms were seen in 27 patients who had not undergone surgical treatment. The locations of these aneurysms are given in Table II.

Absolute measurements of aneurysmal size were unobtainable. It was, however, evident that the visibility of an intracranial aneurysm was greatly dependent on its position. Middle cerebral artery aneurysms were most easily seen. Aneurysms arising at the origin of the posterior communicating artery were the most difficult to identify because of vascular overlap. Aneurysms arising from the ophthalmic, anterior communicating, basilar and internal carotid arteries were intermediate in their conspicuity with intravenous DSA.

DISCUSSION

The value of intravenous DSA depends very much on how individual neurosurgical units manage their patients with intracranial aneurysms. This is illustrated in its use to confirm a CT diagnosis of aneurysm. It is the policy of some neurosurgeons to undertake "prophylactic" surgery on incidentally discovered aneurysms. In such circumstances we feel it is worthwhile to employ intravenous DSA as a simple confirmatory test (Figs 1, 2). Our study demonstrates that intravenous DSA is both safe and reliable when used in this role. The patient then undergoes selective cerebral angiography before surgery. It must be emphasised that we cannot justify initial intravenous DSA in those patients presenting with typical clinical features of subarachnoid haemorrhage.

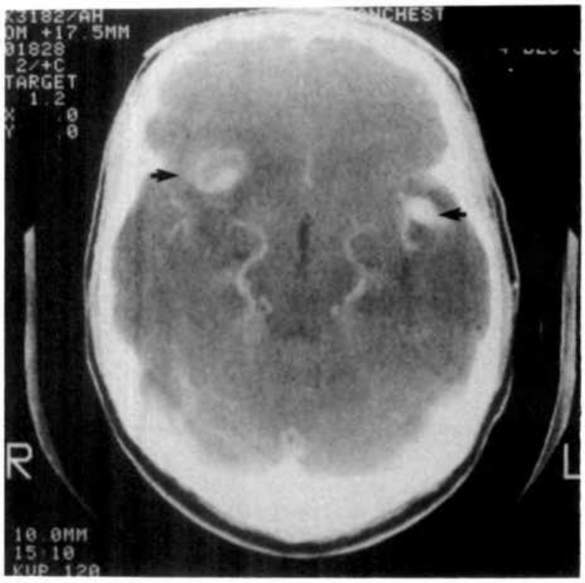

FIG. 1.

Cranial CT (after administration of intravenous contrast medium). Two aneurysms are seen arising from each of the middle cerebral arteries (arrows). Thrombosis is seen within the aneurysmal sac on the right.

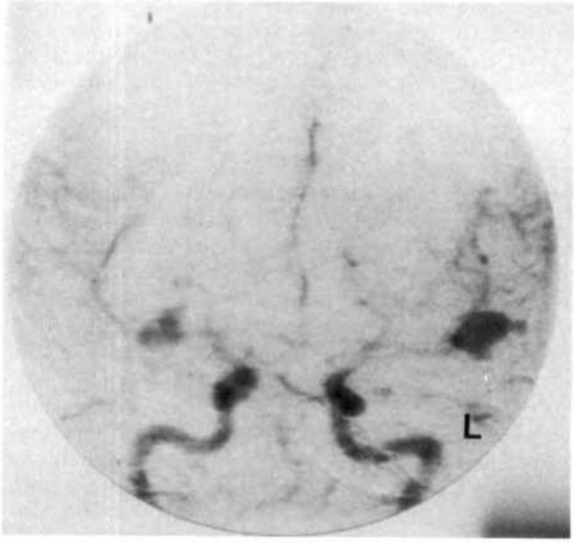

FIG. 2.

Cerebral intravenous DSA, frontal projection. Same patient as in Fig. 1. The two aneurysms are shown, the left having the larger patent lumen.

Spasm of the major intracerebral arteries is clearly seen using intravenous DSA (Figs 3, 4). This dangerous and common sequel of subarachnoid haemorrhage is not readily detected by CT. Aneurysm surgery is aimed at preventing recurrent haemorrhage. Timing of such

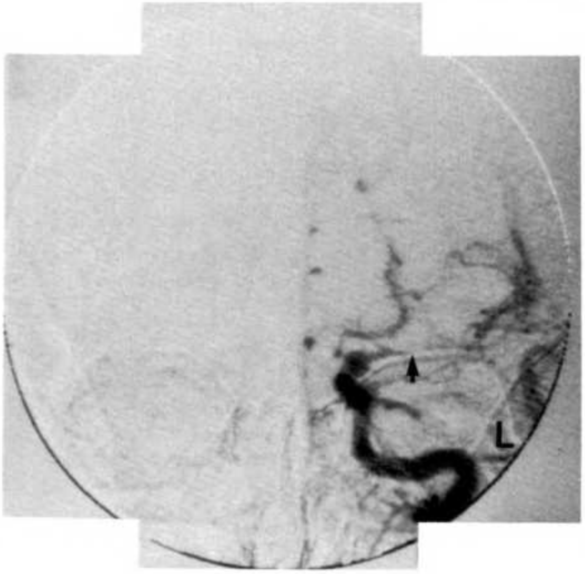

FIG. 3.

Arterial DSA. Left common carotid artery injection. There is marked spasm affecting the left middle cerebral artery (arrow).

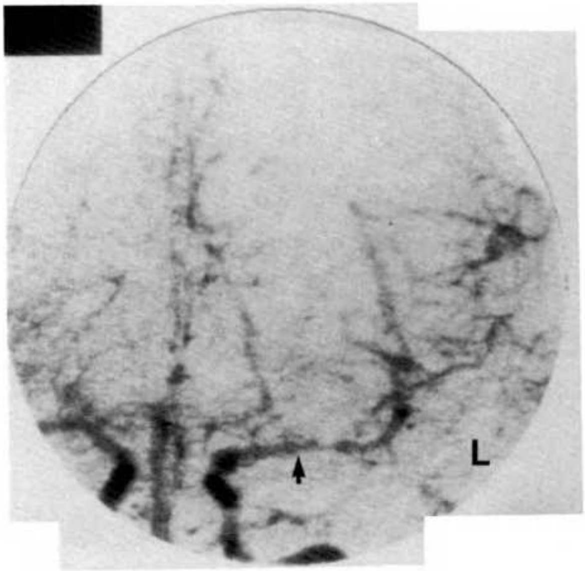

FIG. 4.

Cerebral intravenous DSA, frontal projection. Same patient as in Fig. 3. The left middle cerebral artery spasm has partially regressed (arrow).

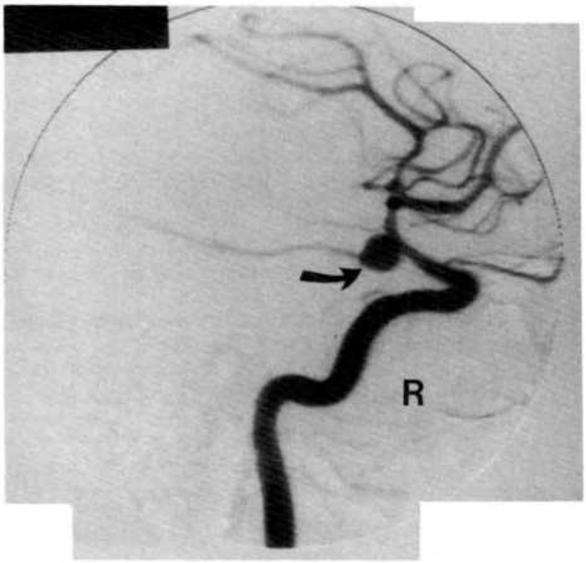

FIG. 5.

Arterial DSA. Right internal carotid artery injection. An aneurysm at the origin of the posterior communicating artery is shown (arrow).

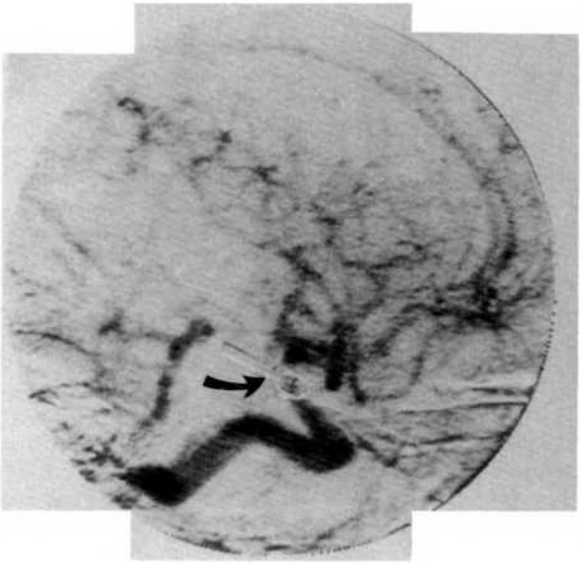

FIG. 6.

Cerebral intravenous DSA, lateral projection. Same patient as in Fig. 5: post-operative study. The clip at the base of the aneurysm is shown partially subtracted (arrow). Obliteration of the aneurysm is complete.

surgery is critical because of the dangers of operating upon patients with clinical or radiological evidence of intracranial arterial spasm (Allcock & Drake, 1965). A decision is reached on clinical grounds, perhaps assisted by repeated CT scanning, as to when surgery should take place. Some patients remain difficult to assess in this way and our experience suggests that the availability of a simple and safe angiographic technique enabling the detection of cerebral artery spasm is of help in these circumstances.

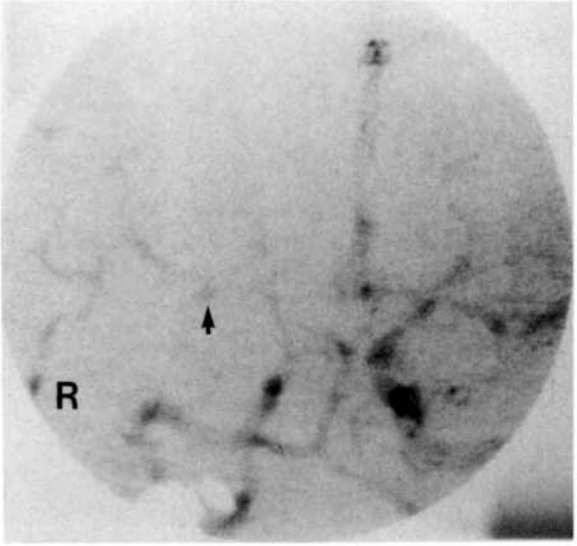

Fig. 7.

Cerebral intravenous DSA, frontal projection. There is partial filling of an incompletely obliterated right middle cerebral artery aneurysm (arrow). Spasm affects the supraclinoid portion of the right internal carotid artery and the proximal segments of the right anterior and middle cerebral arteries.

Individual neurosurgical practice varies with respect to the requirement for post-operative ("check") angiography. Intra-operative judgment regarding aneurysm obliteration is thought reliable by many neurosurgeons, but there is evidence that such assessment may prove unduly optimistic in an appreciable number of cases (Drake et al, 1984). It is known that incomplete obliteration of an aneurysm adversely affects the prognosis (Drake & Vanderlinden, 1967) and that a surgical clip can "slip" from an initially satisfactory position (Drake & Allcock, 1973). Since post-operative arterial angiography carries a slight but not insignificant risk (Mani & Eisenberg, 1978a,b,c) we considered it unjustifiable to compare intra-arterial with intravenous DSA in this post-operative group. However, a favourable comparison between intravenous DSA and intra-operative assessment was observed (Figs 5, 6). The technique shows the adjacent cerebral arteries and whether or not there is persisting spasm (Fig. 7). Intravenous DSA can be carried out in the early post-operative period following major cranial surgery and its simplicity is such that it does not prolong hospital stay.

Patients known to have an intracranial aneurysm can be regularly reviewed using serial intravenous DSA examinations. Gross changes in size can be monitored, including the gradual thrombotic obliteration of an aneurysm following carotid artery ligation, and the projections which show the aneurysm to best advantage on the original angiogram can be repeated for the intravenous study.

We conclude that, in our experience, intravenous DSA has become established as an important part of the radiological management of patients with intracranial aneurysm.

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Identification of intracardiac thrombus: comparison of computed tomography and cross-sectional echocardiography

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ABSTRACT

Thirty-eight patients with conditions predisposing to intracardiac thrombus have been studied by computed tomography and cross-sectional echocardiography. Computed tomography identified 22 cases of intracardiac thrombus (13 left ventricular, eight left atrial and one right atrial). Cross-sectional echocardiography identified five of these left ventricular thrombi and the right atrial thrombus, but none of the left atrial thrombi. In addition, measurements of thrombus density on computed tomography identified a significant difference ($p < 0.02$) between the density of a new compared with an organised thrombus.

Intracardiac thrombus formation can occur in a number of clinical conditions and identification of its presence is important in view of the risks of embolism. As treatment with anticoagulants has inherent complications, many patients at risk are not treated unless a thrombus has been identified or, more often, peripheral embolism has already occurred. The exception to this is mitral-valve disease with atrial fibrillation where left atrial thrombus formation is common and the risk of embolism is high

Cross-sectional echocardiography is an accurate method of detecting left ventricular thrombus (Stratton et al, 1982). Examination of the left atrium and, in particular, its appendage is, however, not as encouraging in this respect (Schweizer et al, 1981) unless transoesophageal echocardiography is employed (Schlüter et al, 1982). In addition, a further, not insignificant problem with echocardiography is in the investigation of patients with lung disease or obesity when a complete study cannot always be obtained (Feigenbaum, 1981, Stratton et al, 1982).

Cardiac computed tomography (CT) provides cross-sectional data of the heart. It should, therefore, be possible to identify a space-occupying lesion in any heart chamber. Previous studies have indicated that CT is an accurate method for detecting intracardiac thrombus (Nair et al, 1981; Tomoda et al, 1983) and one study has indicated that it may be possible to differentiate new from organised thrombus (Tomoda et al, 1980).

Until the introduction of echocardiography, the diagnosis of intracardiac thrombus was based on a clinical supposition, on its likelihood following systemic embolism, or on direct observation at surgery or post-mortem examination. Echocardiography has demonstrated that the incidence of intracardiac thrombus in patients at risk is greater than was formerly suspected. Apart from the selected group of patients who proceed to cardiac surgery, there is at present no independent means of confirming a diagnosis of intracardiac thrombus made by echocardiography or by any other non-invasive technique. In these circumstances it seems reasonable to report our experience in identifying intracardiac thrombus with CT and discuss the findings in relation to echocardiography. We have also attempted, using CT, to differentiate new from organised thrombus.

PATIENTS AND METHODS

Patients

Thirty-eight consecutive patients were studied by CT and cross-sectional echocardiography to identify intracardiac thrombus formation. Thirty-four had predisposing conditions (nine left ventricular aneurysms, 10 global left ventricular dysfunction—both groups diagnosed by angiography—10 mitral-valve disease and five with electrocardiographic evidence of transmural anterior myocardial infarction). The remaining four patients had definite evidence of intracardiac thrombus; three had idiopathic atrial fibrillation with systemic embolism and one patient with a permanent pacemaker had developed central venous obstruction.

The majority of patients were studied prospectively by both techniques. Those patients with left ventricular aneurysms, however, were selected retrospectively. They formed part of a group studied previously by CT for a different purpose and all patients who had had echocardiography within a week of the CT studies were included.

Computed tomography and echocardiography were performed within a 7-day period in all patients and

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anticoagulant therapy had not been started in the intervening time in any patient. The CT scans and echocardiograms were reported blind, each by two experienced independent observers.

Echocardiography

Cross-sectional echocardiography was performed using either a Varian 3400R (28 patients) with a 2.25 MHz phased-array transducer or a Hewlett Packard 77020A ultrasound system (10 patients) with a 3.5 MHz phased-array transducer. Long- and short-axis and apical four-chamber views were performed in all patients and where left ventricular thrombus was suspected a subxiphoid view was also attempted. Presence and site of thrombus were reported, as well as whether any difficulties were encountered in obtaining adequate data because of obesity or lung disease. Thrombus was identified as an area of abnormal high-intensity echoes in a region adjacent to the myocardium. Variation in window level and S curve settings were used to exclude the possibility of artefact.

Computed tomography

The CT studies were performed using an International General Electric 8800 CT/T scanner with dynamic-scan facilities. This has a scan time of 5.6 s and an interscan time of 2.4 s for dynamic incremental studies. The scanner has a spatial resolution of up to 7 line pairs/cm and the contrast resolution is 0.4%. In order to identify the anatomical levels to be scanned during contrast-medium infusion, one scan projection radiograph and two scans at the base and two at the apex of the heart were first performed. An infusion of iodinated contrast medium (Conray 280 (May & Baker) or Hexabrix (May & Baker)) was given into an antecubital vein using a Medrad Mk IV power injector. In the majority of patients 80–100 ml of contrast medium was given at 2 ml/s. The remaining two patients were coincidentally undergoing electrocardiographic gated studies of the left ventricle and contrast medium was given as a bolus of 25 ml at 10 ml/s followed by an infusion at 10 ml/min. Scanning was started 20 s after the start of the contrast-medium infusion which was continued until scanning was completed. Scans (1 cm thick) were performed at 1 cm intervals to image the whole of the left ventricle in those patients with aneurysms and myocardial infarcts, and in the remaining patients scans were performed to include all four heart chambers. All scans were performed during held maximum inspiration.

Thrombus was identified as a filling defect in the opacified cardiac chambers which was seen at two or more levels scanned (Figs 1, 2). In addition to identifying the thrombus, its density in Hounsfield units (HU) was measured, by manually tracing round the thrombus and measuring the mean density in HU within the region of interest using standard computer software. Two groups of patients were identified, those likely to have new thrombus (recent myocardial infarct and recent-onset atrial fibrillation, six patients) and those with organised thrombus (14 patients with long-standing disease). The thrombus densities of the two groups were compared using Student's t-test.

Fourteen of the 24 patients with conditions predisposing to left ventricular thrombus formation were studied by left ventricular angiography as part of their diagnostic investigation. Where a left ventricular filling defect was identified this was noted.

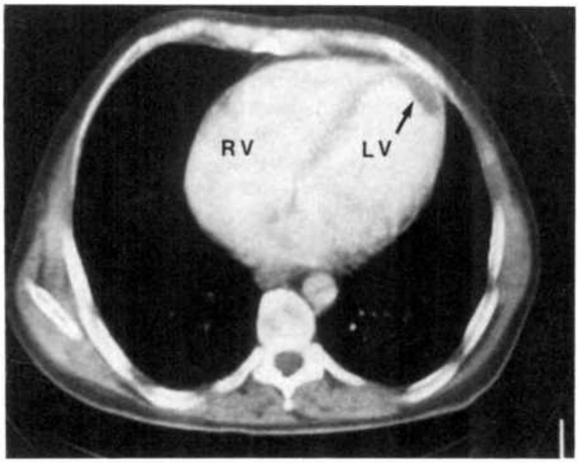

FIG. 1.

Computed tomographic scan of a patient with a left ventricular aneurysm demonstrating thrombus (arrowed) on the anterior wall of the left ventricle. LV, left ventricle; RV, right ventricle.

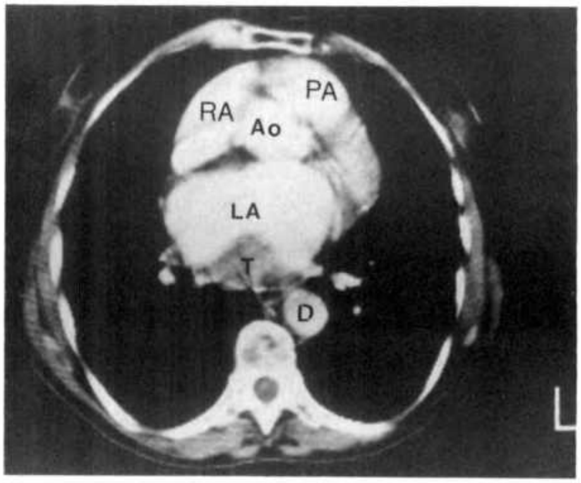

FIG. 2.

Computed tomographic scan demonstrating thrombus in the left atrium. T, thrombus; LA, left atrium; Ao, ascending aorta; PA, pulmonary artery; RA, right atrium; D, descending aorta.

TABLE I

IDENTIFICATION OF THROMBUS BY CT AND ECHOCARDIOGRAPHY RELATED TO DIAGNOSIS

Diagnosis	No. of patients	Computed tomography		Echocardiography	
		Left ventricle	Left atrium	Left ventricle	Left atrium
Left ventricular aneurysm	9	7	–	2	–
Global left ventricular dysfunction	10	2	–	2	–
Mitral-valve disease	10	–	5	–	–
Myocardial infarct	5	4	–	1	–
Idiopathic atrial fibrillation	3	–	3	–	–
Permanent pacemaker	1	–	1*	–	1*

*Right atrium.

RESULTS

Identification of thrombus (Table I)

Cross-sectional echocardiography identified five cases of left ventricular thrombus and a right atrial thrombus complicating a permanent pacemaker lead (confirmed at open-heart surgery).

Computed tomography also demonstrated these cases of intracardiac thrombus and identified a further eight ventricular and eight left atrial filling defects (three left atrial appendage (Fig. 3)) which had the same appearances as in those cases where echocardiography had identified thrombus. In view of this, it was assumed that the filling defects seen on CT were in fact thrombi. The appearances of the filling defects seen in these cases had not been observed in any of a large group of patients (91) with ischaemic heart disease without infarction who had undergone cardiac CT. Left ventricular angiography identified a left ventricular filling defect in an akinetic or aneurysmal area in three cases. A filling defect had been demonstrated by CT in these three cases but not at echocardiography.

In five cases the echocardiographic study was inadequate. In a further 11 cases it was not felt possible to exclude totally an intracardiac thrombus as the examination in these cases was not considered to be completely perfect. These 16 cases included the majority (five of eight) of the cases of left ventricular thrombus identified by CT but not by echocardiography. There was no difference between the findings of the two observers at either CT or echocardiography.

Density of thrombus

It was possible to measure the density of the thrombus in 21 of the 22 cases. In the patient with a right atrial thrombus, artefact from the pacemaker lead made this impossible.

In one patient with atrial fibrillation of unknown duration it was felt impossible, clinically, to assess the age of the thrombus (density 61 HU), and this case was, therefore, excluded from the analysis.

In those cases where the thrombus was thought to be new, the mean density was 34±8 HU, and in those where the thrombus was thought to be organised, the mean density was 51.6±11.5 HU. Comparison of the two groups of measurements showed a significant difference in density ($p < 0.02$).

Of the three patients with systemic emboli, two had thrombus of low density (28 HU and 39 HU) and one patient had a thrombus of high density (61 HU).

DISCUSSION

A major difficulty in the non-invasive investigation of patients with intracardiac thrombus is confirmation of the findings. The ideal comparison would be with pathological data. This is not available, however, in the majority of instances as (1) the conditions predisposing to thrombus formation are not necessarily life threatening and (2) the incidence of surgical intervention in patients not previously treated with anticoagulants is relatively rare. Standard angiographic techniques are not an accurate method for identifying intracardiac

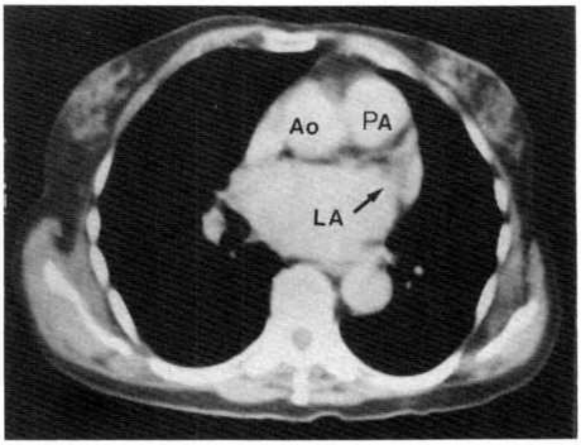

FIG. 3.

Computed tomographic scan demonstrating thrombus (arrowed) in the left atrial appendage. LA, left atrium; Ao, ascending aorta; PA, pulmonary artery.

thrombus (Reeder et al, 1981), presumably because data are available from only one or two projections. If multiple views were possible, the accuracy of this technique should improve. This may be possible using digital subtraction imaging. Although not performed as part of this study, coincidental diagnostic left ventricular angiography identified three cases of thrombus where CT had shown a left ventricular filling defect. In no case in which left ventricular angiography demonstrated a thrombus did CT fail to do so.

Thrombus identification

Assuming echocardiography correctly identifies intracardiac thrombus, CT correctly identified all cases of thrombus visualised by this technique. In addition to these, CT identified a further 15 cases of intracardiac filling defects with the same appearance and density as in those cases where confirmation of thrombus was available.

Without direct inspection of the heart in those patients thought not to have intracardiac thrombus, it is impossible to exclude totally a small thrombus not visualised by either CT or echocardiography. This, however, is unlikely in view of the good spatial resolution and density discrimination of the CT scanner used in this study.

The results obtained from echocardiography are, to a certain extent dependent on the population under study, which will vary depending on the cultural and industrial environment If, as in this study, there is a large percentage of obese patients and patients with lung disease, intracardiac thrombus may not be detected. Where adequate data can be obtained, however, left ventricular thrombus can usually be identified (Stratton et al, 1982). If the CT findings in this study are assumed to be correct, then in those cases where a complete study was possible, echocardiography identified five of the eight cases of left ventricular thrombus.

Echocardiography is not an accurate technique for identifying left atrial thrombus: the highest reported sensitivity is 58% (Shrestha et al, 1983). The major reason for these poor results is the inability of echocardiography to visualise adequately certain areas of the left atrium, in particular the left atrial appendage (Schweizer et al, 1981; Shrestha et al, 1983). One report (Herzog et al, 1984) has shown that it is possible to image thrombi in the left atrial appendage by echocardiography, but no assessment of the sensitivity or specificity of the technique has been made.

Computed tomographic data are obtained from multiple positions around the body for each scan. With the scan time of 5 6 s used in this study, each scan will contain data from a number of cardiac cycles. The majority of data collected will, therefore, be from diastole, when little movement is occurring. Data from systole will be superimposed on this and as contrast medium is used this information will be obscured. Because of these factors, even small areas of the heart, such as the left atrial appendage, are readily visualised. A significant disadvantage of CT is the image artefact produced by any high-density substance. This therefore excludes CT from the identification of thrombus on prosthetic valves.

Thrombus density

New thrombus within the heart is composed mainly of platelets and fibrin and contains fewer red cells and less haemoglobin than either circulating blood or recent haematoma. It will therefore have a lower density on CT than either. Blood, assuming a normal haemoglobin, has a density of 40–50 HU. Organised thrombus, on the other hand, contains a high percentage of fibrous tissue and often has developed a capillary blood supply and, occasionally, even contains calcium. These changes associated with organisation would be expected to increase significantly the density on CT In this study, CT has demonstrated a significant difference between the density of new and organised thrombus. Theoretically, organised thrombus is less likely to embolise than new thrombus, especially if sited in a non-contracting area of the heart. Knowledge of the age of thrombus may therefore be important when considering treatment in individual patients, especially where there is a contraindication to anticoagulant therapy

CONCLUSIONS

The results from this study indicate that CT is an accurate technique for the identification of intracardiac thrombus. In view of the nature of the condition, however, definite confirmation is not available. It has also proved possible to differentiate new from organised thrombus.

Echocardiography, being less invasive, should remain the investigation of choice for the detection of intracardiac thrombus. In those cases, however, where (1) a complete study cannot be obtained, (2) left atrial thrombus is suspected but not identified and (3) in patients with major contraindications to anticoagulant therapy where differentiation of new from organised thrombus would help in management, CT should be the investigation of choice.

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Book reviews

Quantitative Coronary and Left Ventricular Cineangiography. By J. H. C. Reiber, P. W. Serruys and C. J. Slager, pp. 454, 1986 (Martinus Nijhoff, Dordrecht), £74.95.
ISBN 0–89838–760–4
State of the Art in Quantitative Coronary Arteriography. Ed. by J. H. C. Reiber and P. W. Serruys, pp. 274, 1986 (Martinus Nijhoff, Dordrecht), £69.75.
ISBN 0–89838–804–X

When the second of these two books arrived for review—similar title, similar publisher's cover format, and two of the three names on the front the same—I thought there must be some bizarre duplication. However, the two books are very different animals. The first divides into two parts: an extended description and analysis of the authors' own method of computerised analysis of coronary arteriograms and left ventriculograms and a series of research clinical applications of their methods. For coronary arteriograms they digitise the cine frames, apply computerised edge detection to arteries with strictures and left ventricles, and process the results by computer to derive measurements. Readers will be pleased to know that even their sophisticated system requires the human eye to check that the computer is looking at the right part of the artery, and has to be told which bits of the ventricle to analyse. This book is obviously for the dedicated worker in the field who wants to see how the competition does it.

The second book is a multiauthor contribution edited by the same workers as above, and dedicated primarily to the coronary arteries, and in which different groups working in the field describe their own methods, with the results and limitations. It includes a chapter on cine CT. I found it a much wider and more balanced overview and, because of the diversity of approaches, much more interesting to read. For the radiologist, general, vascular, or cardiac, who wants to keep abreast of modern computed image processing in the vascular field, this is a good book. For the enthusiast who wants to enter the field himself, both are required reading.

M. Raphael

Cardiac Doppler Diagnosis, Vol II. Ed by M. P. Spencer, pp. x+244, 1986 (Martinus Nijhoff, Dordrecht), £49.95.
ISBN 0–89838–767–1

This is a small book of approximately 240 pages by multiple authors. Essentially, it is a series of short papers on specific subjects rather than a textbook of Doppler echocardiography. Initially, there is a very personal view of the historical milestones in echocardiography that would probably be of more interest to those of us who have seen the subject grow than to readers who come to the fully developed specialty. Then follow chapters on the physics of Doppler ultrasound, time interval histogram, velocity profiles in the aortic arch and the influence of geometry of the ascending aorta on the velocity profile. All are treated in a mildly mathematical way which is likely to be more appreciated by the physicist than by the clinician. Subsequent chapters on transcutaneous aortovelography and the use of this technique in exercise-testing are followed by chapters on colour-flow Doppler. The remainder of the book is devoted to more clinical papers.

It is not for the novice in the art but will provide interesting further reading for those already well versed in the subject. Many clinicians will find the physics and mathematics beyond them and the non-clinicians may stumble over the somewhat brief clinical explanations. It is not quite clear at whom the book has been directed and the preface does not say, but I suspect that physicists were more in mind than clinicians.

R. B. Pridie

1987, *The British Journal of Radiology*, *60*, 333–341 APRIL 1987

Quantitative tissue characterisation in pancreatic disease using magnetic resonance imaging

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ABSTRACT

Twenty-nine patients, 27 of whom had either inflammatory disease of the pancreas or pancreatic tumour, were studied by magnetic resonance imaging (MRI) and computed tomography (CT). Six healthy volunteers were studied by MRI alone. The pancreatic T_1 and T_2 relaxation times were calculated using a multipoint iterative method with data from seven total saturation recovery and six spin echo sequences. Magnetic resonance imaging can demonstrate the normal pancreas and a variety of pathological processes greater than 1–2 cm in size, but with less spatial resolution than CT. The relaxation-time results indicated no significant discrimination between chronic pancreatitis and pancreatic tumour. A significant elevation in the relaxation times was observed, however, in those patients with calcific chronic pancreatitis compared with the non-calcific chronic pancreatitic group and normal controls, suggesting a different pathophysiology for the two subgroups of chronic pancreatitis. The active phase of acute pancreatitis was associated with significantly elevated relaxation times, which returned to normal levels during the resolved phase of the disease. Associated extrapancreatic fluid collections were characterised by their very long relaxation times. The problems associated with spatial resolution, respiratory motion and lack of quantitative tissue characterisation suggest that MRI of the pancreas, using present methods, is unlikely to contribute to the overall management of patients with exocrine pancreatic disease.

The aim of this study was to assess the role of measured T_1 and T_2 relaxation times in the normal and diseased pancreas using magnetic resonance imaging (MRI). The details of our method (Hickey et al, 1986b; Isherwood et al, 1986) and its validation (Jenkins et al, 1985; Johnson et al, 1986) have already been described. We report our preliminary results.

METHODS

Clinical

Forty-five patients (age range 20–84 years) with known or suspected pancreatic disease were investigated by MRI and dynamic contrast-enhanced computed tomography (CT). In 16 patients the MRI data were unreliable, in 11 because data were obtained early in the development of the method and in five because of the small size of the pancreas (Fig. 1). Quantitative MRI data from the remaining 29 subjects form the basis of this report.

Five patients had *pancreatic cancer*, confirmed at surgery in two and at death in the others. In all patients the tumour was in the head of the pancreas. In addition, a patient with primary adenocarcinoma of the stomach was shown at laparotomy to have direct invasion of the pancreatic tail by tumour. The diagnosis of *chronic pancreatitis* in 16 patients was based principally on the radiological findings of pancreatic calculi and/or abnormal endoscopic pancreatograms and/or reduced exocrine secretory capacity (Braganza et al, 1982). The disease was ascribed to chronic alcoholism in five patients but no cause was identifiable in the remainder. The pancreatographic changes in 13 patients showed "advanced changes" in six, "moderate changes" in five and "minimal changes" in two (Braganza et al, 1982). Pancreatic calculi were detected by CT in 10 patients (calcific CP), the changes being extensive in seven. In this subgroup the average duration of symptoms (mean 5.3, range 2–11 years) was significantly longer than in the subgroup with non-calcific disease (mean 2.5, range 0.5–5.0 years). The diagnosis of *acute pancreatitis* was retained when no evidence of residual pancreatic structural or functional damage was present after complete recovery (Gyr et al, 1984). The active phase of the disease was defined by continuing abdominal pain and elevated serum amylase. The attack of acute pancreatitis in the five patients examined was thought to be precipitated by alcohol in three, related to extensive retroperitoneal lymphadenopathy from non-Hodgkin's lymphoma in one and in the remaining patient no cause was identifiable. Three patients were examined in the active phase of the illness and of these one had already developed extrapancreatic fluid collections and was rescanned 2 months later. The two other patients were examined in the resolved phase at 6 weeks and 72 weeks after the attack.

The control group consisted of six healthy volunteers and two patients with abdominal symptoms which were ascribed to an irritable bowel syndrome when exhaustive pancreatic and gastrointestinal investigations proved negative. The age range in this group was 27–64 years.

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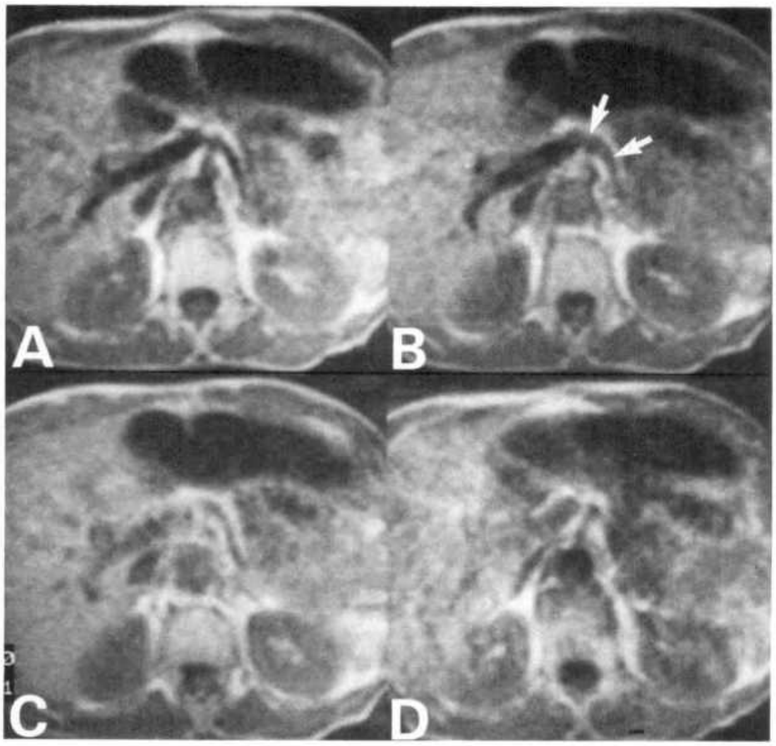

Fig. 1.

Four transverse multisection IR 2080/500 images from (a) inferior to (d) superior. The pancreas, arrowed in (b), is very small in this patient with severe chronic pancreatitis.

Imaging

Computed tomography preceded MRI to optimise the anatomical level for collection of the MRI data. A solution of Gastrografin (Schering AG) (sodium and meglumine diatrizoate, 8 ml in 250 ml water) was given orally 90 min and 15 min before CT. An IGE CT/T 8800 scanner was used with a dynamic scanning sequence before and after intravenous injection of Conray 280 (May & Baker) (100 ml meglumine iothalamate, 280 mg iodine/ml).

The MRI was performed on a Picker International superconducting magnet system operating at 0.26 T. Data were collected in the transverse plane at a single anatomical level through the pancreas, using non-gated sequences. A section thickness of 10 mm was used and the images were obtained using a two-dimensional Fourier transform reconstruction. Data, within a region of interest, from seven total saturation recovery (TSR) sequences (Waterton et al, 1984) and six spin echo (SE) sequences were used to calculate the T_1 and T_2 relaxation times by an iterative least squares method (Hickey et al, 1986b). The corresponding Pearson correlation coefficients (Beaumont, 1972) were obtained for T_1 and T_2. Approximately 50 min per patient was needed to collect the 13 magnetic resonance data images using 64 gradient increments, each with two signal excitations. A typical set of data images is shown in Fig. 2. An additional eight-image multisection sequence (usually inversion recovery (IR) 2080/500, using 128 gradient increments each with two signal excitations) was performed in the sagittal or coronal plane for morphological display of the upper abdomen.

In 15 patients in the early phase of the study, and five volunteers, ferric ammonium citrate BP (28 mg elemental ferric iron in 500 ml water) was used as a paramagnetic oral contrast agent (Wesbey et al, 1983) in an attempt to delineate more clearly the stomach and duodenal loop and to allow separation of these structures from the pancreas. This was not always achieved and for the remainder of the study effervescent tablets (Baritop, Sakai Chemical Industry) and 20 mg hyoscine butylbromide (Buscopan, Boehringer Ingelheim) were given just before the examination.

Statistical methods

The relaxation-time data were first shown to be normally distributed using a Kolmogrov-Smirnov test (Siegel, 1956). Then the T_1 and T_2 relaxation times in the various subgroups were examined by analyses of variance (*F*-tests) for unpaired samples (Moore & Edwards, 1965) and, where appropriate, Student's *t*-tests. Differences were considered significant when $p < 0.05$ and highly significant when $p < 0.01$ using two-tailed tests. Mean values of the relaxation times were quoted with the corresponding standard errors. The T_1 and T_2 values were excluded from the analysis if the Pearson correlation coefficient from the multipoint

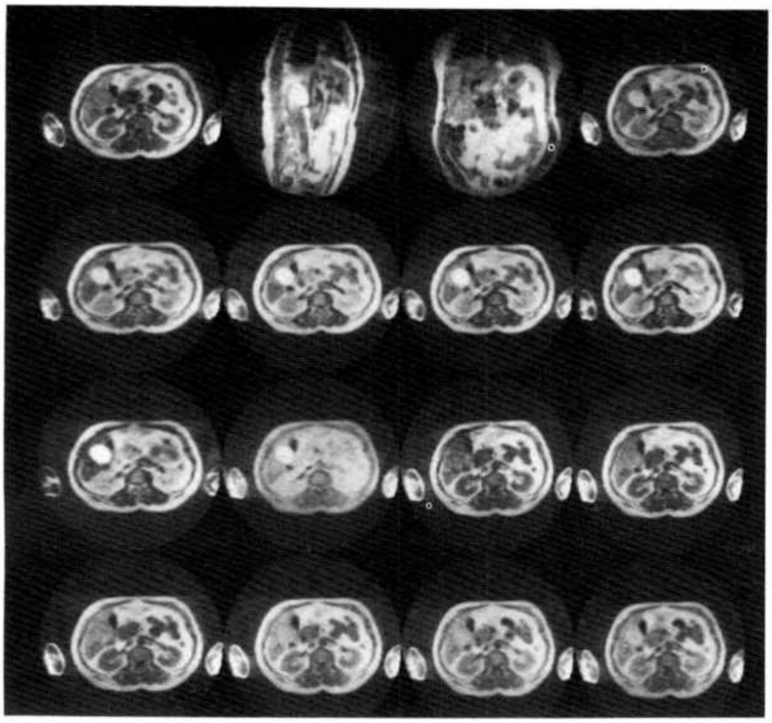

Fig. 2.

A 13-image data set (Frames 4 to 9 SE images and Frames 10 to 16 TSR images) preceded by three siting SE scans.

algorithm was < 0.85; the majority, however, had values > 0.95.

Results

Imaging

Normal pancreas. In the controls the pancreas and major abdominal vessels (aorta, inferior vena cava, superior mesenteric artery and vein, portal and splenic veins) were routinely visualised. The absence of intraluminal signal from rapidly flowing blood provided a high intrinsic contrast between the lumen, vessel wall and surrounding soft tissues. The pancreas appeared as a homogeneous structure on T_1- and T_2-weighted images; in the latter it had a similar signal intensity to liver but in the former the intensity was slightly lower (Fig. 3). Retroperitoneal fat, which gives a high signal on both T_1- and T_2- weighted images, facilitated demarcation of the margin of the pancreas from the adjacent bowel. Difficulty was encountered when retroperitoneal fat was sparse.

Pancreatic disease. Despite an improvement in image quality and definition achieved by reducing bowel peristalsis and distending the stomach and duodenum with gas, small pancreatic lesions and pancreatic calcification (less than 1 cm) were poorly visualised in comparison with CT.

Pancreatic carcinoma. All five lesions were demonstrated using similar morphological criteria as for CT, with focal enlargement and irregularity in outline of the pancreatic head (Fig. 4). Local extension and, in four cases, biliary obstruction were demonstrated, as was involvement of major vessels in two (Fig. 4). None of the cases had evidence of retroperitoneal lymphadenopathy, or metastatic disease. However, liver metastases in one patient with a primary gastric tumour were better demonstrated on MRI compared with unenhanced CT, but were equally well shown on contrast-enhanced CT.

The signal intensity of the pancreas on both T_1- and T_2-weighted images was variable and in two cases similar to the normal gland (Figs 3, 4). One patient had a Silastic endoprosthetic stent *in situ* within the common bile duct which produced no visible artefact on the magnetic resonance images, although streak artefacts were apparent on CT.

Chronic pancreatitis. When the pancreas was small, *i.e.* less than 1 cm thick, as in five cases, it was barely discernible on MRI (Fig. 1). In these cases CT defined the gland more clearly. In the six cases of non-calcific chronic pancreatitis, both T_1- and T_2-weighted images showed normal signal intensities from the pancreas, but in one case a dilated pancreatic duct was seen on MRI. There was slight focal irregularity in outline to parts of the pancreas in two cases, but this feature was more clearly defined by CT.

Only two of the 10 cases with calcific chronic pancreatitis had evidence of calcification seen on MRI, demonstrated as low-intensity regions on both T_1- and T_2-weighted images. In two cases the magnetic resonance images were normal on both morphological

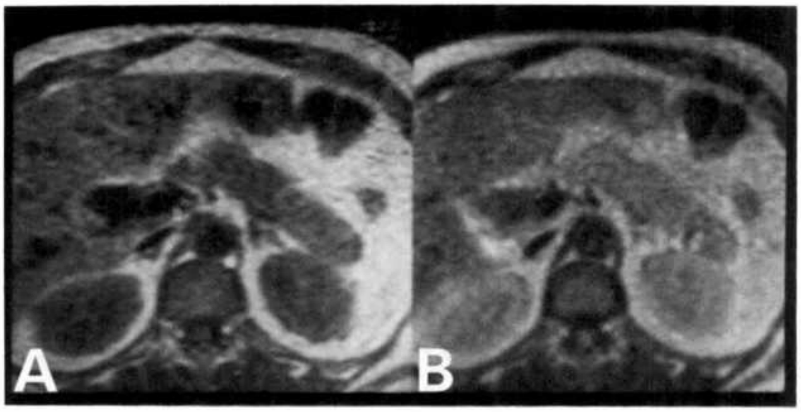

FIG. 3.
Normal pancreas on transverse section. (A) T_1-weighted (TSR 150) and (B) T_2-weighted (SE 1000/60) images.

and signal intensity criteria. In the remaining eight cases, apart from irregularity in outline which was better demonstrated on CT, both T_1- and T_2-weighted images showed a heterogeneous signal intensity from the pancreas. Extrapancreatic fluid collections were noted in two cases, one surrounding the spleen and one in the anterior pararenal region. Fat infiltration of the liver and an enlarged pancreatic duct were demonstrated with CT but were not seen with MRI using conventional sequences. Surgical clips produced no visible MRI artefact.

Acute pancreatitis. In the group with acute pancreatitis the images depended on the stage at which the magnetic resonance scan was performed. In the three cases examined in the active phase the pancreas was diffusely enlarged on both CT and MRI. A normal signal intensity to the gland was noted on MRI in two cases (Fig. 5), while the other exhibited an heterogeneous appearance on T_2-weighted images. In the patient with lymphoma, the enlarged pancreas was separated by a fat-plane from the retroperitoneal lymphadenopathy, which showed a similar signal intensity. In this case the pancreatic duct was noted to be slightly enlarged on CT, but was not seen on MRI. The pancreas appeared normal in the three cases examined in the resolved phase. Extrapancreatic fluid collections, noted in two cases, were more easily detectable and were more clearly outlined on contrast-enhanced CT.

Relaxation times

The results are summarised in Table I with the individual T_1 and T_2 values in Figs 6 and 7. In the group of five pancreatic carcinomas there was no significant difference in the T_1 or T_2 values compared with the group of eight controls. However, in a patient with a well circumscribed tumour in the head of the pancreas (Fig. 4), both the T_1 (875 ms) and T_2 (74 ms) values were higher than the highest value in the controls; whereas both values from the morphologically normal pancreatic body and tail, in the same patient ($T_1 = 596$ ms, $T_2 = 61$ ms) (Fig. 3), were within the control range. Another patient with a primary adenocarcinoma of the stomach (not included in Table I or Figs 6 and 7) and liver secondaries, however, had localised enlargement of the tail of the pancreas owing to direct spread of the gastric cancer; T_1 (524 ms)

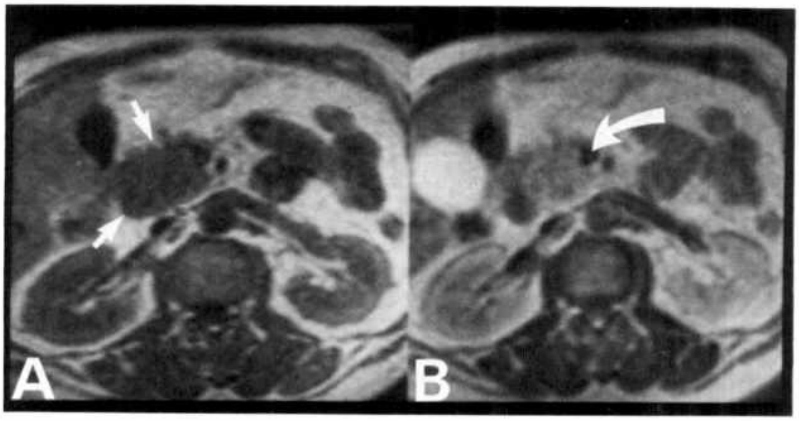

FIG. 4.
(A) T_1-weighted (IR 2080/500) and (B) T_2-weighted (SE 1000/60) transverse images showing irregular enlargement of the head of the pancreas (straight arrows) from a carcinoma. There is encasement of the superior mesenteric vein (curved arrow). Note the homogeneous signal intensity from the pancreas on both images, similar to Fig. 3. The signal from the gallbladder contents in (A) and (B) is related to the relatively short T_1/long T_2 from concentrated bile in a fasting patient.

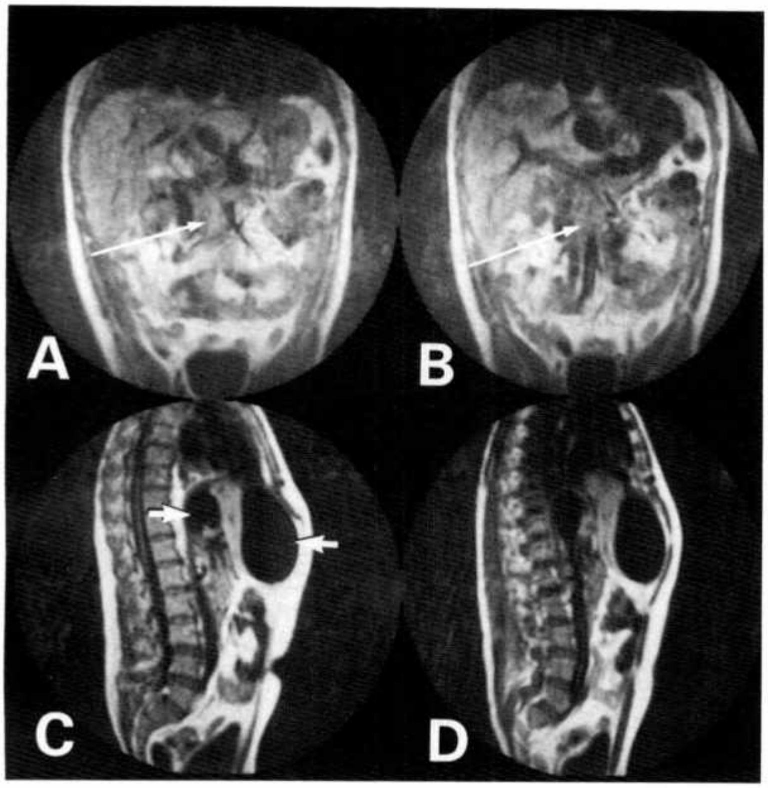

FIG. 5.

Four IR 2080/500 images from two multiset sequences, (A) and (B) coronal, and (C) and (D) sagittal, in a patient with acute pancreatitis in the acute phase associated with multiple extrapancreatic fluid collections. The enlarged pancreas is shown in (A) and (B) (arrowed). Two extrapancreatic fluid collections are noted in (C) (arrowed) and (D), the anterior one being subcapsular and compressing the right lobe of the liver.

and T_2 (66 ms) values from the tail of the pancreas were within the range of the control group.

Chronic pancreatitis. Analyses of variance showed that there were no significant differences in 16 patients with chronic pancreatitis ($T_1 = 682 \pm 54$ ms; $T_2 = 61 \pm 3$ ms) in their T_1 ($F = 0.75$; $p > 0.05$) or T_2 ($F = 1.69$; $p > 0.05$) values compared with the control, pancreatic tumour and active and resolved acute pancreatitic groups. Further analyses, however, revealed significant differences in the relaxation times of the subgroups with calcific and non-calcific chronic pancreatitis separated for both T_1 ($F = 2.67$; $p < 0.05$) and T_2 ($F = 2.78$; $p < 0.05$). Student's *t*-tests confirmed that the mean T_1 value in the subgroup with calcific chronic pancreatitis (773 ± 40 ms) was significantly higher than the mean value in the subgroup with non-calcific disease (523 ± 94 ms; $p < 0.05$), or the mean value in the controls (544 ± 40 ms; $p < 0.01$). There was a significant difference ($p < 0.05$) in the T_2 values of the calcific chronic pancreatitis patients (66 ± 3 ms) compared with controls (56 ± 3 ms), but no difference when compared with the non-calcific group (56 ± 7 ms). In seven of the 10 patients with calcific chronic pancreatitis, extensive calcification was present throughout the pancreas ($T_1 = 827 \pm 41$ ms; $T_2 = 66 \pm 4$ ms). Small flecks of calcium in the pancreas were found on CT in the remaining patients. In one of these, T_1 values were obtained from both the head of the pancreas, which contained the calcium flecks, and the pancreatic body, which was enlarged and showed heterogeneous contrast enhancement on CT but no calculi; in the former region the T_1 value was 707 ms, which was just greater than the maximum value in the control group (T_1 range = 330–692 ms), while in the latter region it was raised, at 997 ms. Extrapancreatic fluid collections were noted in two of the 10 patients with calcific

TABLE I

MEAN T_1 AND T_2 VALUES WITH STANDARD ERRORS (SE) FOR NORMAL AND DISEASED PANCREATIC TISSUE

	No. of cases	Mean T_1 $\pm$SE (ms)	Mean T_2 $\pm$SE (ms)
Normal controls	8	*544 ± 40	†*56 ± 3
Pancreatic tumour	5	676 ± 77	65 ± 7
Chronic pancreatitis:			
Calcific	10	†*773 ± 40	†66 ± 3
Non-calcific	6	†523 ± 94	56 ± 7
Acute pancreatitis:			
Active phase	3	608 ± 139	*72 ± 3
Resolved phase	3	636 ± 31	*46 ± 3

*Highly significant difference ($p < 0.01$). †Significant difference ($p < 0.05$).

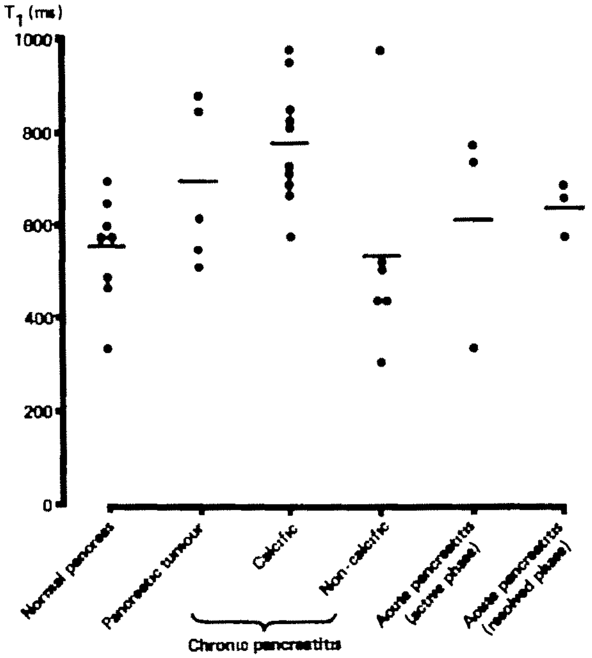

FIG. 6

T_1 values (including means) for normal and diseased pancreatic tissues.

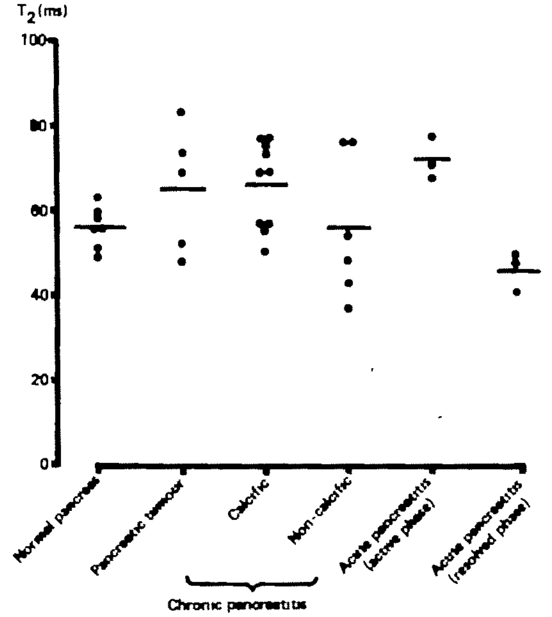

FIG. 7.

T_2 values (including means) for normal and diseased pancreatic tissues

chronic pancreatitis and the relaxation times, measured in one, were elevated (T_1 = 1317 ms, T_2 = 99 ms).

In the patients with chronic pancreatitis an attempt was made to examine the relaxation times in relation to presumed aetiology, prevailing pancreatic exocrine function and pancreatographic appearances whenever this information was available. The relaxation times in five patients with alcohol-related disease (T_1 = 804±52 ms; T_2 = 67±5 ms) and 11 patients with idiopathic disease (T_1 = 626±69 ms; T_2 = 67±5 ms) were not significantly different ($p > 0.05$). There was no correlation of the relaxation times with grading of disease as assessed on endoscopic pancreatographic criteria. Pancreatic function tests were abnormal in all but one of the group with calcific chronic pancreatitis, but only half of the non-calcific cases.

Acute pancreatitis. The individual T_1 values in the three patients with active disease were 759 ms, 736 ms and 330 ms, while their T_2 values were 71 ms, 77 ms and 68 ms, respectively. Because of the low T_1 value of 330 ms in the patient with extrapancreatic fluid collections, the mean T_1 of this subgroup (608±139 ms) was not significantly different from the control mean (see Table I). However, the mean T_2 value of 72±3 ms represented a highly significant increase above the control mean ($p < 0.01$). In the patient with lymphoma, the relaxation times from the retroperitoneal lymphadenopathy (T_1 = 699 ms; T_2 = 68 ms) were similar to the values obtained from the enlarged pancreas (T_1 = 736 ms; T_2 = 77 ms).

Three patients were examined 6, 8 and 72 weeks after the acute attack; while the T_1 values in this subgroup did not differ from any other group (Table I), the T_2 values (46±3 ms) were significantly less ($p < 0.01$) than the subgroup of acute pancreatitis in the active phase (T_2 = 72±5 ms).

In two patients, extrapancreatic fluid collections were noted, one in the active phase and the other in the resolved phase of the disease; in both patients T_1 (3083 ms and 4640 ms) and T_2 (170 ms and 237 ms) values were markedly elevated, in keeping with the cystic nature of these fluid collections.

DISCUSSION

Direct comparison of the few published reports on MRI of the pancreas is difficult because of differences in methods and presentation of the data. Smith et al (1982), using a low-field (0.04 T) resistive system in 12 patients, suggested that not only could MRI detect pancreatic disease but that T_1 measurements facilitated differential diagnosis. However, in that study the pancreas was not visualised in patients without evidence of pancreatic disease. Rupp et al (1983), using a 0.2 T resistive system, recorded T_1 and T_2 relaxation times, but from the data presented it was impossible to gauge the range of values in the various diagnostic subgroups; the authors concluded that pancreatic carcinoma and pseudocyst were associated with elevated T_1 while pancreatitis was associated with elevation in T_2. These same results were quoted by Anacker et al (1984). Stark et al (1984), using a 0.35 T superconducting magnet system, were less optimistic about the discriminatory value of MRI, reporting wide variations in relaxation times measured in each disease subgroup. No pancreatic relaxation time data were presented by Haaga (1984).

We have used a robust and reproducible multiple data point method which was designed to eliminate some of the technical errors in relaxation time measurement (Jenkins et al, 1985; Hickey et al, 1986b; Isherwood et al, 1986). Even in this preliminary study, the striking feature was the wide variation in T_1 values in both the normal and the diseased pancreas. Before discussing the possible significance of the two other principal findings—the significant increase in T_1 in patients with calcific CP and the significant increase in T_2 in the active phase of acute pancreatitis, shown in Table I—it is necessary to consider the limited quantitative tissue characterisation of normal, neoplastic or inflamed pancreatic tissue by MRI.

Relaxation times vary with magnetic field strength (Koenig et al, 1984), the imaging instrument and the method used for their measurement (Mathur-de Vré, 1984, Hickey et al, 1986b) Thus, we have shown experimentally (Hickey et al, 1986b) and confirmed in other clinical situations (Jenkins et al, 1985; Johnson et al, 1986; Hickey et al, 1986a) that the use of several data points in describing T_1 and T_2 exponentials gives greater discrimination than when the relaxation times are derived from only two points, as in the hitherto reported studies in pancreatic disease (Smith et al, 1982; Rupp et al, 1983; Stark et al, 1984). The lack of increased discrimination, despite the improved measurement technique and the routine use of a bowel relaxing agent to reduce peristalsis, in our current study is probably the result of several factors. Firstly, pancreatic excursion during respiration and the influence of cardiac motion combine to reduce spatial resolution and produce movement artefacts. While this may be rectifiable by gating techniques, such modification would increase patient scanning time. Secondly, the pancreas lies in an oblique plane, giving rise to partial volume effects in the numerical information. Thirdly, the positioning of regions of interest (ROIs) used to calculate the T_1 and T_2 values is subject to observer error in a 13-image data set. Pixel distribution of T_1 and T_2 in the form of tissue maps and in the two-dimensional probability arrays provide more information in the characterisation of tissues compared with ROIs (Conners & Harlow, 1980; Hickey et al, 1986a; Isherwood et al, 1987) and their use in future pancreatic studies should reduce this source of error.

The fast-proton diffusion model (Fullerton et al, 1982) suggests that T_1 of tissues is dominated by two factors: the total water content, and the ability of tissue macromolecules (mainly proteins) to bind water in the hydration layer (*i.e.* water molecules that are loosely bound to, or associated with, macromolecules so that their motion is restricted). These factors have a weak influence on T_2 which, however, is strongly affected by the concentration of crystalline water-binding sites (*i.e.* water that is tightly bound within macromolecules) as well as by the thickness of the hydration water multilayer Small changes in water content, typically of a few per cent, cause large variations in T_1 values (Mansfield & Morris, 1982). Variations in the macromolecular structure of tissues will result in differences in the amount of hydration water and their binding characteristics (Fullerton et al, 1982).

Acute pancreatitis in the active phase is characterised by an outpouring of fluid from the vascular compartments into the gland. There is loss of the normal partitioning of pancreatic secretions so that much less than normal passes into the duodenum, while much more exudes from the surface of the gland into the peripancreatic tissues. This pattern occurs irrespective of the presumed aetiological factor and, likewise, rapid resolution of the attack both in morphological (pancreatic size) and functional (normal serum amylase) terms is to be expected in the majority of cases. However, after recovery, the biochemical changes within the pancreas are likely to differ greatly, depending on the trigger factor. Thus, where a migrating gallstone is the apparent culprit, pancreatic exocrine function may be normal when tested 6 weeks later, but when alcoholism is the apparent cause hypersecretion of pancreatic protein and bicarbonate may be discovered (Burton et al, 1960; Dreiling et al, 1973). The elevation in T_2 in the active phase of pancreatitis is probably explained by interstitial oedema resulting in an increased concentration of crystalline water-binding sites in addition to the thickness of the hydration water multilayer, an explanation which is supported by the rapid fall in the T_2 value in a patient who was re-examined during the recovery phase. The outflow obstruction to pancreatic secretions in the active phase may explain the raised T_1 values in two patients (759 ms and 736 ms), an interpretation supported by the low T_1 value (333 ms) in another patient who was also studied in the active phase but who showed extensive extrapancreatic collections of pancreatic secretions that had probably escaped from the surface of the gland. The formation of extensive extrapancreatic collections is associated with a favourable sparing effect on the pancreas, which often exhibits only mild oedema (Siegelman et al, 1980).

Extrapancreatic fluid collections were characterised by their very long T_1 and T_2 values: the two associated with acute pancreatitis (one in the active and the other in the resolved phase) had values more than double the one associated with chronic pancreatitis. This variation in relaxation times probably reflects the biological variation to be expected with different concentrations of solutes within the fluid collections.

Hypersecretion of various constituents (protein/bicarbonate/mucus/calcium) is characteristic of chronic pancreatitis in the earliest phases (for bibliography see Braganza, 1986). This phenomenon has been best described in the context of alcohol-related disease which tends to affect the larger draining ducts of the gland so that the pancreatogram is often grossly abnormal. In our practice, chronic alcoholism can be incriminated in less than 50% of patients and, in this group, a wide range of morphological and/or functional disturbances may be found. Although there is a broad correlation between the degree of abnormality on the pancreatogram and the degree of reduction in pancreatic exocrine secretory capacity in patients with chronic pancreatitis as a whole, occasionally wide discrepancies are found (Braganza et al, 1982). Thus, small-duct disease characterised by a normal or equivocal pancreatogram is not infrequently accompanied by reduction in exocrine (particularly bicarbonate) secretory capacity. By contrast, a grossly abnormal main pancreatic duct with pancreatic calculi may be accompanied by a pancreatic function profile that is at the upper limit of the reference range. Sarles (1984) envisaged all forms of the disease as progressing eventually to calcification, hence advocating the all-embracing term "calcifying chronic pancreatitis" which may be the case when, as in Sarles' practice, the disease is largely seen in chronic alcoholics. However, in patients with idiopathic disease, who constitute 50% of our practice, it is not uncommon to find diffuse calculi in young, non-alcoholic patients presenting with a short history of 1–2 years; nor at the other end of the spectrum is it uncommon to find no evidence of calcification in patients who have been followed for up to 30 years. The patchy nature of the lesions (acinar atrophy, periductal fibrosis, protein plugs in ducts, ductal distortion) and the unpredictable course of the disease, however, are not in dispute.

Chronic pancreatitis is typically punctuated by episodes of active pancreatitis and it is, therefore, not surprising that the range of T_1 and T_2 values was so wide in the 16 patients studied (Figs 6, 7). What is surprising, however, is that despite the biological variations, both the T_1 and T_2 relaxation times in the subgroup with calcific disease significantly exceeded the respective values in controls, and in the case of T_1 was significantly higher compared with the subgroup with non-calcific disease. This difference is not spurious and does not appear to be related to the prior administration of contrast medium for CT. Loss of free bulk water is a possible consequence of contrast medium administration and would be expected to *reduce* the T_1 relaxation time (Fullerton et al, 1982). Calcium itself gives no MRI signal and therefore the increased T_1 in the patients with calcific chronic pancreatitis cannot be ascribed directly to the presence of calculi. This argument is supported, in one patient, by the lower T_1 value, 707 ms, from the head of the pancreas, which contained calcific flecks, compared with the T_1 value of 997 ms from the body of the pancreas, which contained no visible calculi on CT. Therefore, it seems that the process of hypersecretion of protein and mucus is the explanation. The only patient currently characterised as having non-calcific chronic pancreatitis, in whom the T_1 value of 967 ms is clearly excessive, is being monitored for the development of pancreatic calculi. The much lower values in the patients in the subgroup with non-calcific disease suggest either that the pathogenesis in this subgroup does not involve hypersecretion of macromolecules or that the gland was completely fibrosed with no surviving acinar glands. The latter explanation is unlikely, as half of these cases had normal pancreatic function tests and, indeed, the relaxation times were within the control range in the majority

Finally, MRI, even with quantitative tissue characterisation, is disappointing in the context of pancreatic carcinoma: neither is the distinction between tumour and chronic pancreatitis possible, nor, indeed, is it possible to say with certainty from the T_1 or T_2 values whether a neoplasm from a neighbouring organ, including lymphoma, has infiltrated the gland The ability to monitor recovery from attacks of acute pancreatitis must be weighed against the high cost and long patient scanning time with MRI.

CONCLUSION

Magnetic resonance imaging can demonstrate the normal pancreas and a variety of pathological processes, if of sufficient size to alter the normal contour, but with less spatial resolution than CT. Improvements in spatial resolution are to be expected with the use of surface coil imaging, faster pulse sequences or gating techniques which do not have significant time penalties.

Relaxation times reflect the water content and the dynamic structure of water in different tissues. Our preliminary study of patients with exocrine pancreatic disease demonstrates these general principles. In the active phase of acute pancreatitis, characterised by pancreatic oedema with alteration in the partitioning of secretory constituents, T_1 and T_2 relaxation times tend to be elevated. A differential effect on the T_1 and T_2 values probably reflects the varied circumstances in which the disease is produced and the associated alteration of the water structure and binding characteristics. Hypersecretion of pancreatic exocrine constituents and involvement of the large ducts of the pancreas is characteristic of the earliest phases of calcific chronic pancreatitis, the pathophysiology of which seems to be indicated by a significant increase in T_1 values. The separation in T_1 values in patients with non-calcific chronic pancreatitis, compared with the calcific group, perhaps reflects a different pathophysiological basis. Pancreatic tumour cannot be differentiated from chronic pancreatitis on T_1 and T_2 measurements, nor can their use predict whether or not the gland has been infiltrated by a tumour from adjacent organs. It remains to be seen whether further refinements in technology, including the use of tissue mapping, will greatly alter these conclusions.

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Book reviews

Invasive Radiology. Clinics in Gastroenterology, Vol. 14, No 2, Guest Editor T. A S Buist, pp 295–487, 1985 (W B. Saunders, London), £13.50.
ISSN 0300–5089

This is an excellent little book that has been written by radiologists for gastroenterologists It acts as a companion to a previous text, in the same series, that examined the place of non-invasive diagnostic methods in gastroenterological practice. This examines the place of invasive or interventional procedures in modern practice, and both volumes are part of a series of quarterly hardback publications of gastrointestinal topics available on subscription.

British radiologists would be aware on opening the first page that this would be a thorough examination of current practice. The clue lies with the choice of guest editor, T.A.S (Mike) Buist, who pioneered many of these procedures in Britain and who had developed a worldwide reputation for his skill and painstaking expertise in this field. Many readers will be aware of his recent death at an early age, and British radiology has lost a true ambassador and mentor. He has, however, left us with this volume as one legacy, and has assembled a fine list of contributors, most of whom are acknowledged doyens in their particular subject, and the text reflects their expertise

There is no attempt to describe the technical methods involved, but the emphasis is upon the value of each technique, with an outline of the limitations and complications of each procedure.

The book is divided into three segments. vascular procedures, diagnostic and therapeutic biliary procedures, and percutaneous biopsy and abscess drainage techniques Each segment is subdivided into three or four chapters, each written by a different author. There is no detectable repetition and the illustrations are of excellent quality, but the occasional original radiograph has not led to good reproduction.

The outstanding section to me was the vascular one and, in particular, the chapter on pancreatic angiography, a difficult diagnostic area which has become a much less confused topic after 15 minutes of analysis by Professor Lunderquist

I find it a pity that this book was submitted for review over 18 months after publication, and time has already overtaken some of the topics. Some present procedures of interest are, of course, not mentioned I refer to oesophageal dilatation under fluoroscopic control, percutaneous gastrostomy and jejunostomy, CT angiography and the explosion of techniques of endoscopic endoprosthesis insertion which will largely supersede the percutaneous placement techniques

This is an excellent volume and should be available in all libraries for reference; but it was written for gastroenterologists, and radiologists will need to consult more comprehensive texts for practical help with their daily problems.

As a general overview of the subject by the experts, however, it is unsurpassed and is worth every penny of the price.

Henry W Loose

NMR in Living Systems. By T. Axenrod and C. Ceccarelli, pp 410, 1986 (D Reidel Publishing Co., Dordrecht), £44.50
ISBN 90–277–2174–2

NMR in Living Systems is largely compiled from lectures given at a NATO Advanced Study Institute held in Italy during September 1984. Containing 25 articles and published well over a year after the meeting, like many of such volumes the result is a mixture of several useful articles with some contributions rather hastily put together and, by now, out of date. I enjoyed the introductory and largely historical article by Fish and Becker and found most of the chapters on cellular biochemistry (mainly ^{13}C NMR and study of intracellular ions) helpful. Over 40% of the book is concerned with basic theory and NMR methodology and some of the theory chapters are extensive and heavy going. While it could be argued that not all the theory presented is all that helpful for *NMR in Living Systems*, maybe exposure to quantum mechanical calculations of nuclear shielding tensors is good education After all, Advanced Study Institutes are more for learning in depth than for being brought up to date in the field. To this extent, the volume is clearly different in emphasis and style from many other books with similar titles. For example, there are some practical chapters. *e g* cost and availability of commercial equipment or "how to cope with the NMR literature", as well as contributions on non-medical applications of NMR imaging and other (*i e.* non-NMR) methods for imaging the human body

I suspect that the Study Institute was more helpful to the participants than the published volume will be to readers as I find it hard to see who will want to read the book from cover to cover; yet many people will wish to study individual chapters and use them as a guideline for further study.

The photo-offset production is from rather dense type and much reduced. It is definitely a book for the young who, in good daylight and without special reading glasses or bifocals, will find it easier to concentrate on the content.

G K Radda

1987, *The British Journal of Radiology*, *60*, 343–346 APRIL 1987

Clinical use of Hexabrix for radiological evaluation of leakage from the upper gastrointestinal tract based on experimental study

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ABSTRACT

The clinical use of Hexabrix (May and Baker) was started about 3.5 years ago for the radiological evaluation of patients in whom the possibility of leakage of contrast medium outside the upper gastrointestinal tract, particularly the oesophagus, was anticipated. The majority (> 70%) of the patients were in their early post-operative period. No adverse reactions because of the use of Hexabrix were encountered.

Which contrast medium to use in cases of suspected leakage from the gastrointestinal tract is a question which continues to be asked because of the lack of an ideal medium for radiological examination in such clinical situations as perforations of the upper gastrointestinal tract (GIT), in particular the oesophagus. This question is relevant, not only to spontaneous or iatrogenic perforations of the oesophagus, but, in recent years, to the post-operative radiological assessment often required following advanced oesophageal surgery.

The choice of contrast medium in such cases poses several important questions as to its safety and suitability. Apart from its suitable imaging properties, the contrast medium ideally should not cause any damage to tissues with which it comes in contact, nor produce immediate, early or late toxic effects.

The tissue reaction to several contrast media was experimentally evaluated in the rat bronchi and lungs (Ginai et al, 1984), mediastinum (Ginai et al, 1985), peritoneum (Ginai, 1985) and pleura (Ginai, 1986). The results of these studies showed that the low-osmolality contrast media Hexabrix (May and Baker), Amipaque (Nycomed UK Ltd) and, later, Omnipaque (Nycomed UK Ltd) caused the least reaction when all the various tissues were taken into account. The use of Hexabrix was started clinically in November 1982. To date, over 400 upper GIT examinations with Hexabrix have been carried out and no untoward reactions have been encountered. This article deals with the experiences of the use of Hexabrix in the upper GIT in the first 2-year period, November 1982–November 1984.

PATIENTS AND METHOD

Records were kept of the contrast agent used for all examinations of the upper GIT performed in the 2-year period starting November 1982. One hundred and sixty-seven patients had a Hexabrix swallow examination. The patients (113 men and 54 women), aged 15–95 years, for whom the radiographs and/or video recordings of Hexabrix examinations were available were reviewed. The following data were used for analysis: age and sex of the patient, clinical diagnosis and (if post-operative) the nature of surgery, indication for Hexabrix swallow, diagnostic quality and density of contrast on the radiographs and any recorded side-effects ascribable to the contrast medium.

Method of examination

The patients were examined in the horizontal, semi-erect and/or erect positions, depending on their physical condition and indications. Efforts were made to obtain a minimum of two right-angle views using as small an amount of contrast medium as possible. Hexabrix 320 mg I/ml was used in all oesophageal examinations in the series. The amount of contrast medium used usually varied between 20 ml and 50 ml but occasionally up to 100 ml was used. If severe aspiration was noted with the first swallow (which in cases of clinical suspicion was made in the lateral position for early recognition) the examination was either stopped if the information gained was adequate, or repeated with a second swallow for further information only if absolutely essential. Large quantities of contrast medium were never used in such cases and a video recording was employed in order not to miss any useful information in difficult situations. In post-operative cases, the Hexabrix swallow was performed at about the eighth post-operative day, and if an anastomotic leakage was found, a repeat examination was carried out after a further 4–7 days, initially with Hexabrix. Plain radiographs were often taken before the contrast medium was used and late radiographs were obtained 15 min–60 min after Hexabrix swallow in case of a doubtful leakage. The diagnosis in such cases was almost always made on a combination of fluoroscopy (and in some cases video recordings) and radiographs.

The indications for the use of Hexabrix as the initial contrast medium in the present series were as follows.

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(1) Post-operative (around eighth post-operative day) after oesophageal (75 patients) or pharyngeal and laryngeal surgery (40 patients) (total 115 patients).

(2) After certain endoscopic procedures where leakage could be suspected, including laser myotomy for Zenker's diverticulum (five patients), prosthetic tube insertion as palliative measure in patients with inoperable oesophageal carcinoma (14 patients), removal of foreign body (two patients) and dilatation of stricture (one patient) (total 22 patients).

(3) Miscellaneous indications including iatrogenic perforations of the oesophagus, *e.g.* foreign body in oesophagus or after lye (caustic soda) ingestion, and in patients with very narrow strictures of the oesophagus in whom severe aspiration could be anticipated, as also with certain abnormalities of the swallowing mechanism (total 30 patients).

RESULTS

No adverse reactions were encountered because of the use of Hexabrix 320 in the upper GIT when used in the quantities and method described. The significant abnormal findings are listed as: leakages into the mediastinum or soft tissues, 17; pulmonary aspiration, 25; oesophago-bronchio-tracheo-pleural fistulae, eight; filling of abscess cavity in soft tissue of the neck or lung apex, four.

The radiographs were judged on the basis of the contrast density and diagnostic quality and varied from "excellent" to "acceptable" for diagnosis in 128 patients (Figs 1, 2, 3, 4). Nineteen patients had only a video recording of the Hexabrix swallow, and were all "good" to "diagnostic" in quality. Twenty patients had "barely-diagnostic" to "poor" quality radiographs, but fluoroscopy had helped to reach the correct diagnostic conclusion in most of these cases. However, in one patient with a celestin prosthetic tube, an oesophago-bronchial fistula was missed and was not seen even in retrospect on the radiographs. In another post-operative patient with intrathoracic oesophago-gastric anastomosis, a leakage of contrast medium was not demonstrated, but was later shown as a large oesophago-pleural leak on CT. Apart from these two patients, no false negatives were noted. Many of the mediastinal leakages in the patients with post-operative anastomoses were tiny (pocketed) and most of these were not present on repeat examination. Only a minority of the patients required repeat examinations but the patient with the oesophago-pleural fistula had to be examined several times, as the fistula did not appear to close even after surgery (Fig. 5).

DISCUSSION

The radiologist has a vital role to play in the important diagnosis of perforation of the oesophagus and its localisation. The most important factor in reducing morbidity and mortality in oesophageal rupture is early diagnosis and immediate surgical intervention, a view supported by a large number of

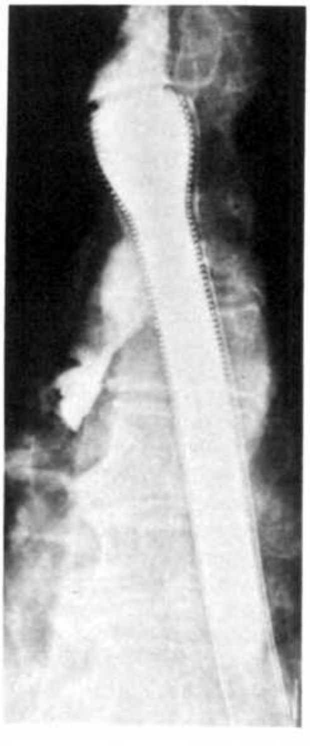

FIG. 1 (*left*).

Hexabrix swallow showing perforation, with contrast medium in the mediastinum on the right side of a prosthetic (celestin) oesophageal tube inserted endoscopically as palliative therapy for inoperable oesophageal carcinoma.

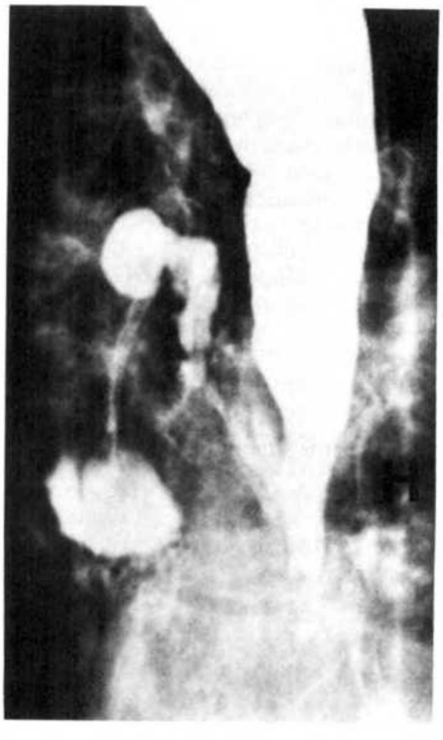

FIG. 2 (*right*).

A 38-year-old man with a perforation of the oesophagus at the site of an old caustic-soda stricture. The perforation was accidently induced by the patient while pushing the food through the strictured oesophagus with a metallic wire (a habit he had acquired a long time ago to relieve food obstruction!). Hexabrix swallow shows leakage of contrast medium into the mediastinum to the right at the site of perforation with a narrow stricture distally and a rather wide obstructed proximal oesophagus.

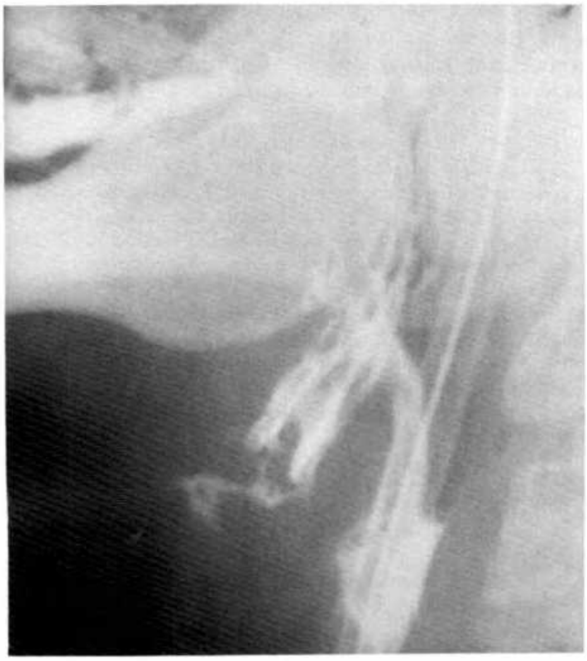

FIG. 3.

A small leakage is shown on Hexabrix swallow in the soft tissues of the neck, below the mandible in a patient who had had a recent total larynx extirpation.

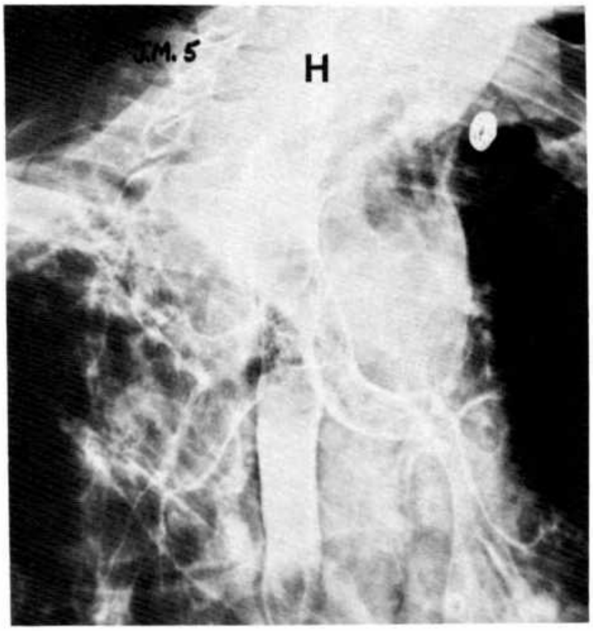

FIG. 4.

Hexabrix swallow showing severe aspiration in a 78-year-old patient with an abnormal swallowing mechanism secondary to chronic subdural haematoma.

publications in the literature (Vessal et al, 1975). Fluoroscopy using contrast medium is of great assistance in providing the necessary information and an ideal contrast medium for use in such cases of leakage should have the following qualities.

(1) It should have adequate radio-opacity.
(2) If aspirated into the lungs in small quantities, it should not cause any immediate or long-term toxic reactions.
(3) If leakage occurs into the mediastinum or soft tissues (*e.g.* of the neck), it should not cause any immediate or long-term toxic effects.
(4) Should it enter the pleural or peritoneal cavity, it should, again, not cause any significant short- or long-term reactions.
(5) It should be palatable for the patient when used orally.

Because the literature contained no complete study on the tissue reactions of the available contrast media in these various sites, we carried out an experimental study on rats (Ginai et al, 1984; Ginai, 1985; Ginai et al, 1985; Ginai, 1986).

Barium sulphate is an ideal contrast medium for routine visualisation of the intact GIT, owing to its superior radiographic density and chemical inertness. Free barium sulphate in the peritoneal cavity, however, causes an immediate inflammatory reaction and subsequently leads to the formation of granulomas. Within a few hours, free intraperitoneal barium sulphate is entrapped in, and cannot be removed from, the peritoneum or serosal surfaces (Zheutlin et al, 1952). Pure barium sulphate, according to some authors (Revill, 1971), causes less reaction because of lack of coating agents and additives. It appeared, however, to cause a similar tissue reaction as commercial barium sulphate in the experimental work carried out on the peritoneum of rats (Ginai, 1985). Encapsulation of barium sulphate in scar tissue, fibrotic adhesions and granuloma formation was clearly seen in the animal studies and has been described in the literature as the cause of eventual intestinal obstruction and mortality (Zheutlin et al, 1952) or urethral obstruction (Herrington, 1966), even long after the initial exposure.

Gastrografin (Schering AG) appears to have several disadvantages due to its high osmolality ($\simeq 1900$ mosmol/kg water), the most serious being the possibility of fatal pulmonary oedema if aspirated into the lungs (Ansell, 1968; Chiu & Gambach, 1974). Experimentally too, Gastrografin has been known to cause serious or significant reaction in the rat lung (Frech et al, 1970; Ginai et al, 1984).

Hexabrix is a water-soluble contrast medium which is a 2 : 1 mixture of meglumine and sodium salts of ioxaglic acid, a monoacid dimer of two benzene rings with six iodine atoms attached. At a concentration of 320 mg I/ml, Hexabrix has an osmolality approximately twice that of blood (Grainger, 1979). The non-ionic

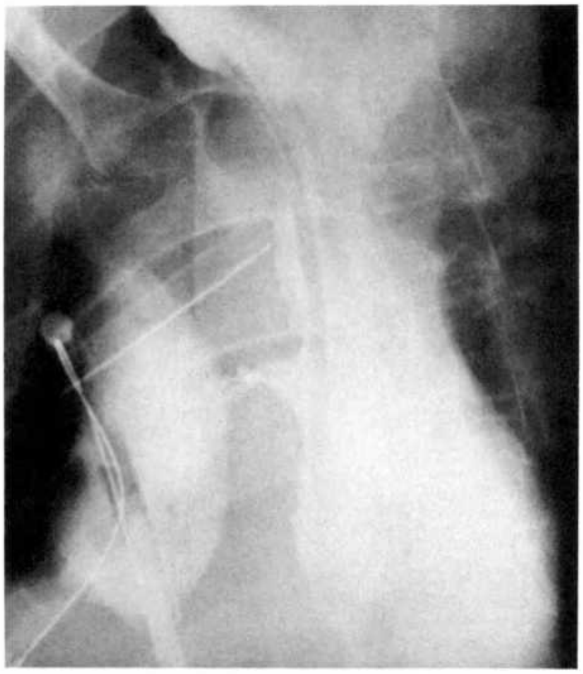

Fig. 5.

Hexabrix swallow in a patient with right pneumonectomy and an oesophagopleural fistula seen at the tip of a traction diverticulum. The right chest cavity is filled with air and fluid containing contrast medium. A drainage tube is also seen. There is a feeding tube in the oesophagus.

contrast media Amipaque and Omnipaque also have an osmolality about twice that of plasma at concentrations of 300 mg I/ml. Because of their low osmolality, Hexabrix and the non-ionic media Amipaque and Omnipaque and possibly also other, newer lower-osmolality contrast media (*e.g.* Niopam, Bracco) would appear to be suitable for use in any circumstances where leakage from the GIT is suspected and aspiration is an accompanying risk.

Conclusion

On the basis of the experimental study on the tissue reaction of various contrast media in lungs, bronchi, mediastinum, pleura and peritoneum of rats, Hexabrix and Amipaque appeared to be the safest media, taking all these tissues into account. The use of Hexabrix, because of its availability as a ready-to-administer solution, began about 3½ years ago for the evaluation of patients with the possibility of leakage outside the upper GIT. The use of Hexabrix in the first 2-year period has been evaluated and has shown no adverse effects attributable to the contrast medium with the quantities and the technique of examination employed.

Hexabrix, or possibly another low-osmolality contrast medium such as the non-ionic Omnipaque or Amipaque, should therefore be the contrast medium of choice for initial radiological evaluation in cases of leakage from the upper GIT. If such an initial study demonstrates no evidence of leakage, the use of a commercial barium-sulphate suspension for further examination would then be justified.

Acknowledgments

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Cortical blindness in toxaemia of pregnancy: findings on computed tomography

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ABSTRACT

Two patients with toxaemia of pregnancy presented with cortical blindness Immediate cranial computed tomography (CT) demonstrated bilateral hypodense areas in the occipital lobes. Both patients underwent Caesarean section for delivery There was gradual and complete recovery of vision, together with CT documentation of resolution of the cerebral changes, indicative of the reversible nature of the ischaemic lesion.

In toxaemia of pregnancy, the neurological complications often reported are impairment of consciousness, seizures and motor deficits (Pritchard & MacDonald, 1980). Cortical blindness as the sole feature is rarely encountered. To our knowledge, the appearance on computed tomography (CT) has been described in only two patients with cortical blindness and impaired conscious level (Beeson & Duda, 1982; Colosimo et al, 1985) We now report the serial CT findings in two patients presenting with cortical blindness alone and discuss the correlations between CT and the pathological changes.

CASE REPORTS

Case 1

A 32-year-old primigravida was admitted at the 30th week of pregnancy because of hypertension and moderate proteinuria The diagnosis of pre-eclampsia was made and she was given the "lytic cocktail" Four hours after admission, she complained of a moderately severe headache and marked visual impairment She was alert and lucid Visual acuity was only light perception in both eyes Fundal examination revealed a small retinal haemorrhage at 3 o'clock in the left eye while the rest of the retina and optic disc were normal Both pupils were 4 mm in diameter and reactive to light and accommodation. The rest of the nervous system was normal. Blood pressure was 180/100 mm Hg. Computed tomography performed 6 h after the onset of blindness revealed bilateral, nearly symmetrical low-attenuation areas in the occipital lobes, involving both the grey and the white matter (Fig 1A) Wedge-shaped hypodensities without mass effect were also noted over both posterior temporal regions. There was mild cerebral swelling, with narrowing of the ventricles and cisterns Urgent Caesarean section was performed and a premature baby weighing 900 g was delivered. The hypertension was controlled with hydrallazine infusion Her visual acuity began to improve on the third post-operative day, with full recovery in 3 weeks A repeat scan 5 weeks later showed complete resolution of the lesions (Fig. 1B)

Case 2

A 33-year-old primigravida was admitted to the maternity ward with the diagnosis of pre-eclampsia, as evidenced by proteinuria, mild oedema and a blood pressure of 190/120 mm Hg. On the day of the scheduled Caesarean section at the 38th week of pregnancy, she woke up with a diffuse headache and bilateral, marked blurring of vision On examination, the visual acuity was only light perception in both eyes, while the fundi and pupillary reactions were normal. No other neurological deficits were elicited Computed tomography demonstrated bilateral, asymmetrical low-attenuation areas in the occipital lobes (Fig 2A). A healthy male baby was delivered by Caesarean section. Hypertension was controlled with intravenous hydrallazine and oral propranolol, and subsequently antihypertensive drugs were taken off Her vision started to improve 3 days after the onset of symptoms and recovered completely in 2 weeks. A repeat CT scan 4 weeks later revealed resolution of previous changes (Fig. 2B).

DISCUSSION

Toxaemia of pregnancy (pre-eclampsia or eclampsia) is a syndrome consisting of arterial hypertension in or beyond the 24th week of pregnancy, accompanied by oedema or significant proteinuria. Symptoms of pre-eclampsia range from mild to severe, and in the latter case there may be cerebral or visual disturbance. When convulsions occur in the absence of pre-existing epilepsy, eclampsia is diagnosed. While the exact cause of the syndrome remains obscure, the most effective treatment for the clinical condition is termination of pregnancy.

Blindness is an uncommon premonitory symptom of eclampsia, with an incidence of 1–3% (Dieckman, 1952). It is mainly attributed to retinal abnormalities, especially retinal vascular thrombosis, retinal oedema and retinal detachment (Carpenter et al, 1953). Pituitary apoplexy presenting with severe visual impairment and headache may rarely occur in patients with a relatively asymptomatic pituitary tumour which enlarges during pregnancy. Visual loss can sometimes be cortical in origin and should always be considered

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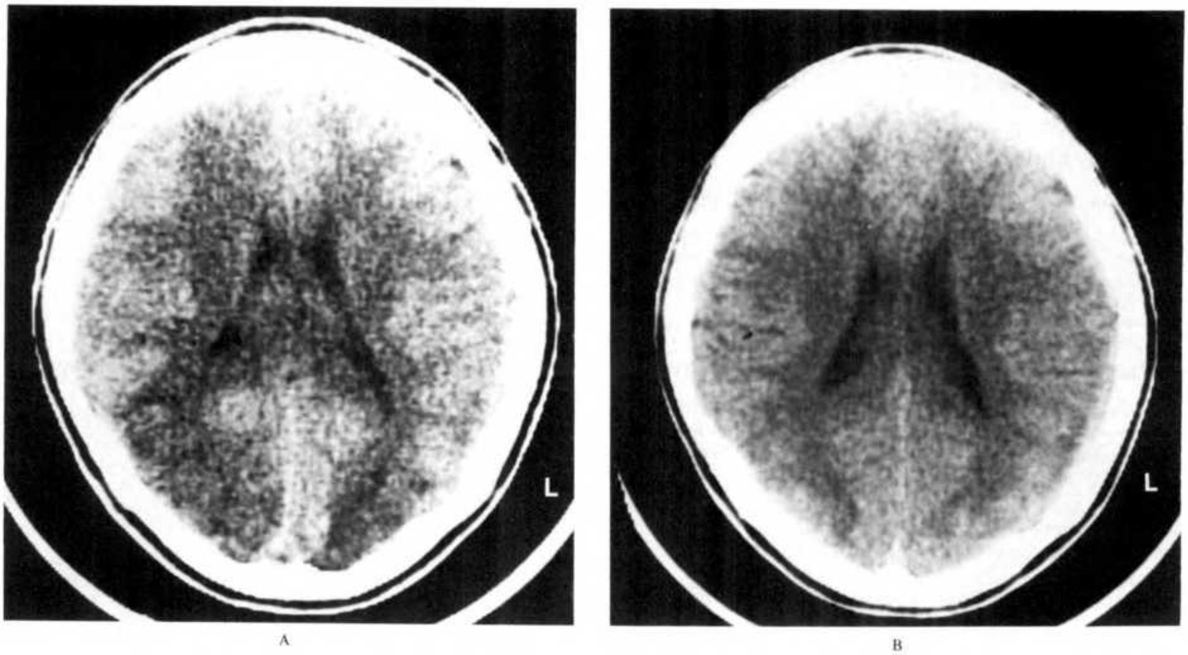
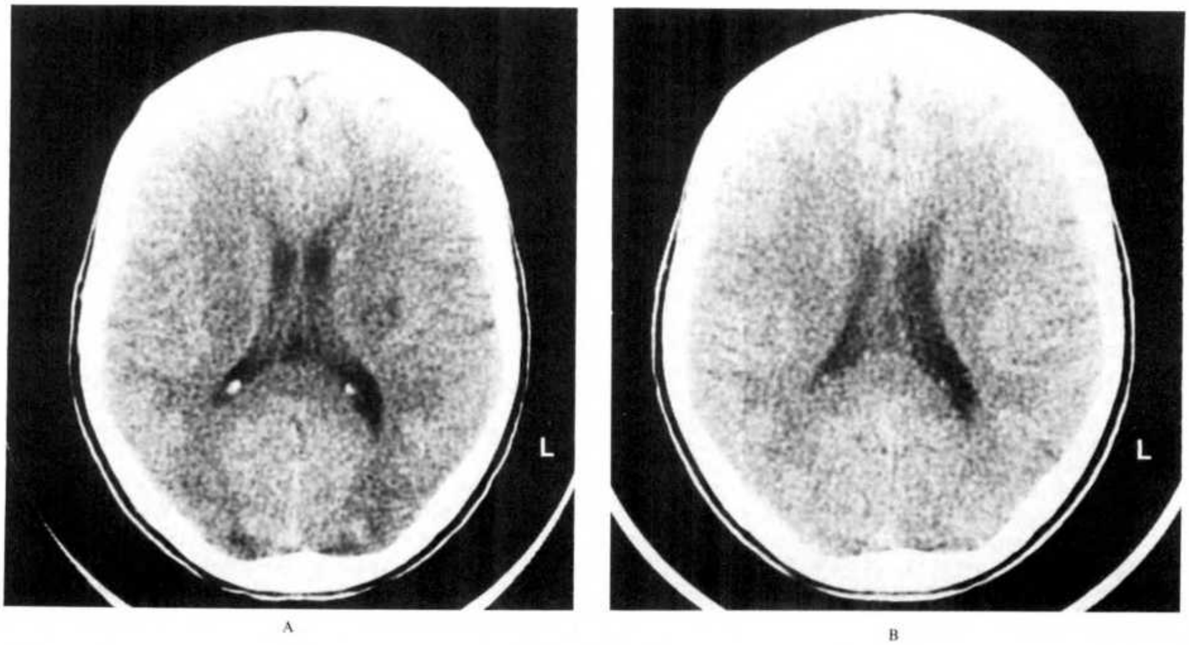


A B

FIG. 1. *Case 1.*

(A) CT scan during the acute stage showed bilateral, almost symmetrical, hypodensities in the occipital lobes. (B) 5 weeks later, follow-up CT demonstrates complete resolution of the occipital hypodensities. Ventricular size is slightly greater suggesting that some compression by brain swelling was present in the acute phase.



A B

FIG. 2. *Case 2.*

(A) Bilateral occipital lobe hypodensities without significant mass effect during the acute phase. (B) Normal findings in the follow-up CT 6 weeks later.

when the pupillary reactions are normal in a blind patient. Our patients presented with cortical blindness and CT provided excellent clinico-anatomical correlation by demonstrating bilateral hypodense areas in the occipital lobes.

Autopsies in fatal cases of eclampsia have consistently demonstrated cerebral oedema, localised intravascular thrombosis, subarachnoid and cerebral haemorrhages (Pritchard & MacDonald, 1980). It has been postulated that some undefined vaso-active substances released from the placenta produce the pathological changes in the brain and other organs by inducing arteriolar spasm (Danforth, 1977). In fact the changes are similar to those seen in hypertensive encephalopathy where disturbance of autoregulation of cerebral blood flow leads either to vasospasm or hyperperfusion (Strandgaard et al, 1973).

Both cerebral oedema and cerebral haemorrhage have been evident in the changes on CT in eclampsia (Colosimo et al, 1985) Cerebral oedema has been classified into vasogenic, ischaemic, cytotoxic and periventricular types (Drayer & Rosenbaum, 1979). Our two patients demonstrated bilateral, symmetrical low-attenuation areas in the occipital lobes during the acute phase, with involvement of both the white matter and cerebral cortex. This obscured pattern of posterior polar changes is suggestive of bilateral ischaemic lesions, perhaps with an additional vasogenic component, and may be related to alterations in the basilar artery circulation. Furthermore, all these changes were completely reversible, as evidenced by their disappearance on the repeat CT scan coupled with full clinical recovery, indicating that altered vascular permeability with resulting accumulation of plasma filtrate is the main pathological event.

In the evaluation of sudden visual loss in toxaemia of pregnancy, CT is helpful in showing the characteristic features of cortical blindness, as well as excluding other intracranial lesions. While cortical blindness is an alarming symptom, the patient can be reassured of the excellent prognosis for complete recovery, which can be documented by regression of the CT changes.

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Book reviews

Lumbar Myelography With Water-Soluble Contrast Media. By M Langlotz, ed. and translated by A E. Oestreich, pp. xii+266, 1986 (Georg Thieme Verlag, Stuttgart), DM198
ISBN 3-13-688301-2 (Stuttgart)
0-86577-228-2 (New York)

In this monograph the place of lumbar myelography is assessed relative to that of modern computed tomography. The author stresses the recent technical advances made in myelography, with the advent of newer non-ionic contrast media and the use of very thin lumbar puncture needles making it a much less traumatic procedure than previously. Its particular advantages as a high-resolution, primarily longitudinal imaging modality with high intrathecal contrast discrimination and the possibility of a dynamic approach are stressed; it is evident that the author's particular interest lies in this modality, though the advantages of high-resolution computed tomography are also stated.

The monograph is presented in two parts, a brief text and an atlas In the latter the radiographs and myelograms are of excellent quality; the computed tomograms are 5 mm sections of reasonable quality. Over 25% of the radiological diagnoses presented in the atlas are not supported by operative or pathological evidence, this detracts from the teaching value of these cases, particularly as some of the images may be regarded as showing ambiguous features.

Minor, more specific criticisms could include "extradural" means outside the dura and not "between two layers of the dura mater", as stated by the author The conus medullaris is, by definition, a point, and it cannot therefore "originate at the level of the first lumbar disc space and terminate at the lower border of the second lumbar body". Adequate evidence is not given for the statement that "nerve root pouch cysts and megacauda may be symptomatic", and the ambiguous statement that "pathological fracture is not distinguished from osteoporotic collapse" needs qualification In the reviewer's experience, the pedicles bordering the widened canal of diastematomyelia are not usually flattened, as is claimed

Such minor criticism would not substantially detract from the value of the book, but, unfortunately, the type of material presented is already available in standard modern texts of neuroradiology The book has no real advantage over these texts for radiologists in training and it contains little to interest practising neuroradiologists.

B. E. KENDALL

Subarachnoid Haemorrhage. By R. P Sengupta and V L. McAllister, pp. x+378, 1986 (Springer Verlag, Berlin), £114.00
ISBN 3-540-15534-1 (Berlin)
0-387-15534-1 (New York)

This is a well written and beautifully illustrated book by a very experienced neurosurgeon and a leading neuroradiologist It provides a comprehensive account of subarachnoid haemorrhage based on the authors' management of over a thousand cases, related to an extensive review of the literature.

Clinical features and the differential diagnosis, the pathology and the abnormalities which are demonstrated by radiological methods, using mainly conventional magnification angiography and computed tomography, the medical management at all stages and the more definitive therapies are considered in detail The unsolved problem of vascular spasm in subarachnoid haemorrhage and its relation to ischaemia is reviewed briefly from experimental and clinical aspects. Special problems, including subarachnoid haemorrhage in pregnancy, childhood and of spinal origin are also considered.

It is possible to make only minor criticisms. Even though spinal dural arteriovenous fistula draining into perimedullary veins rarely presents with subarachnoid haemorrhage, it is the commonest spinal arteriovenous shunt and it should be included in any classification of spinal angiomas The place of embolisation in treatment of intracerebral angiomatous malformations has not yet been established, but any account of it should refer to the excellent results achieved by the French groups—Picard, Moret and Lasjaunias, and Manelfe. It is regrettable that the authors did not have more personal experience of digital angiography and magnetic resonance imaging and had, therefore, to make a less authoritative assessment of the potential contribution of these modalities. These minimal adverse comments are not meant to detract from a book which must become a reference work for radiologists and all neuroscientists, as well as general physicians who deal with the early management of subarachnoid haemorrhage. For this purpose, thorough referencing and a good index are included, but the easily readable style makes it suitable for straight-through, cover-to-cover reading for students seeking a deeper knowledge of the subject

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Electron microscopy of ultrasound-guided fine-needle biopsy specimens

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ABSTRACT

A prospective 3-year study was undertaken in order to assess the value of electron microscopy (EM) as a supplement to routine light microscopy (LM) in ultrasound-guided fine-needle biopsy of suspected abdominal and retroperitoneal tumours. Eighty-six of the 899 ultrasound-guided fine-needle biopsies performed during this period were supplemented with EM using the following indications (1) metastatic lesions with unknown primary tumour, (2) primary retroperitoneal tumours, (3) tumours with atypical clinical histories and (4) where the primary LM evaluation was unable to determine tumour cell type Two methods of obtaining material for EM were tested, namely, fine-needle aspiration and fine-needle histological biopsy (Surecut). Both methods yielded suitable material for EM evaluation in approximately 80% of the 76 cases where tumour cells were identified by LM However, it was technically easier to process material for EM when obtained by fine-needle histological biopsy The results of the 62 cases where suitable material for EM was obtained were grouped according to the histopathological and clinical value of the diagnosis. In 23 cases (37%) EM was without additional diagnostic value. In 12 cases (19%), EM supplied a more precise histopathological diagnosis, but the diagnostic gain was without clinical significance. In 27 cases (44%) EM was of significant clinical value, as the diagnosis by itself was enough to change the investigative procedure and/or the treatment of the patient

Ultrasound-guided fine-needle biopsy of abdominal and retroperitoneal tumours with subsequent evaluation by light microscopy (LM) is regarded as a safe and inexpensive investigative procedure, with a high diagnostic sensitivity and specificity with regard to a malignant diagnosis (Holm et al, 1985). However, in a small proportion of cases, LM is unable to distinguish between different types of malignant neoplasms. As a correct diagnosis of the tumour cell type can be of crucial importance with respect to prognosis and treatment, additional histopathological techniques are indicated. At present, two supplementary methods of investigation of tumours unclassifiable by routine LM are available, namely immunohistochemistry and electron microscopy (EM). Though methods for the routine application of immunohistochemistry to aspirated material are not yet available, several studies have demonstrated the feasibility of performing EM on material obtained by fine-needle biopsy (Hagelqvist, 1978; Akhtar et al, 1981; Kindblom, 1983; Sehested et al, 1983).

The present consecutive, prospective study was, therefore, undertaken in order to determine whether EM of ultrasound-guided fine-needle biopsy specimens could supply a more precise and clinically valuable diagnosis in cases where this was indicated by the LM appearance of the aspirate or by the clinical history. Furthermore, we wished to assess two methods of obtaining material for EM by fine-needle biopsy, namely by aspiration (needle diameter 0.6 mm) and by histological fine needle (Surecut, needle diameter 0 6 mm).

MATERIAL AND METHODS

Patients

The patients were those in whom abdominal or retroperitoneal tumour was detected during the course of an ultrasound examination. All patients were examined at the Department of Ultrasound, Herlev University Hospital, during the 3-year period from October 1982 to October 1985. In all cases material was obtained from the tumorous lesions for LM evaluation, during the first half of the study by aspiration cytology alone and in the latter half of the study by both aspiration cytology and fine-needle histological biopsy (Surecut) (Torp-Pedersen et al, 1984) In both procedures the needles had an external diameter of 0.6 mm. In addition to the LM evaluation, material was obtained for EM when at least one of the following conditions was fulfilled: (1) metastatic lesions where the location and nature of the primary tumour was unknown, (2) tumours located primarily in the retroperitoneum, (3) tumours where the clinical history was atypical and (4) tumours where the primary LM evaluation was unable to determine the tumour cell type. In the latter case a repeat biopsy was necessary, while in the first three cases the material for EM was obtained at the same time as that for LM.

Method of obtaining material for electron microscopy

Material obtained by aspiration biopsy was ejected into a 1.5 ml plastic conical centrifugation tube (Micro Test Tubes, Polypropylene, Milian Instruments SA, Geneva) containing Karnovsky's medium (Karnovsky, 1965) instead of onto a glass slide After fixation for at least 2 h, the aspirate was pelleted at 1400*g* for 30 min.

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The pellet was rinsed in 0.1 M Na-cacodylate buffer, pH 7.4, for 1–2 h or overnight. The pellet was thereafter post-fixed in 1% OsO_4 in 0.2 M S-collidine buffer, pH 7.2, for 1–2 h and then dehydrated in graded ethanol. During dehydration the pellet loosened from the plastic centrifugation tube and could be picked up and transferred through propylene oxide to Epon and finally polymerised. Sections 1 μm thick were cut, stained with toluidine blue, and examined by LM. Ultrathin sections were then cut from areas containing tumour tissue.

Material obtained by fine-needle histological biopsy (Surecut) was also placed into plastic tubes containing Karnovsky's medium as described above. However, the embedding procedure described above could be performed without centrifugation since the material obtained by the Surecut needle consisted of thin tissue cores visible to the naked eye.

The gain in histopathological specificity together with the clinical value of the EM diagnosis of the tumour tissue was classified into three groups. The first group consisted of cases where the EM diagnosis did not add to the LM diagnosis. The second group included cases where the EM examination led to a more specific histopathological diagnosis than that of LM alone, but where this further knowledge was without actual clinical value to the patient. The third group included cases where the EM evaluation not only led to a more specific histopathological diagnosis, but also was of significant clinical value. An EM diagnosis with significant clinical value was defined as being of sufficient importance, by itself, to change the investigative procedure and/or treatment of the particular patient

RESULTS

The major part of the material obtained for EM in the whole study was from the liver (33 cases), the retroperitoneal space (25 cases), the pancreas (10 cases) and the adrenal gland (four cases). In the remaining 14 cases the material had been obtained from a variety of organs (spleen, kidney, bladder) or from loosely defined areas (omentum, left iliac fossa, pelvis).

Material for EM was obtained by aspiration in the first half of the study from 34 patients and by the histological fine needle in the second half of the study from 52 patients.

In the first group of 34 patients, no tumour cells were detected by LM evaluation in three cases. In the remaining 31 cases suitable material for EM evaluation was found in 24 cases (77%), while the aspirated material was too necrotic in six cases (19%) and in one case no tumour cells were detected in the material obtained for EM, though found in the material obtained for LM.

In the second group of 52 patients, no tumour cells were found by LM evaluation in seven cases. In the remaining 45 cases suitable material for EM evaluation was available in 38 cases (84%) while the material was too necrotic in three cases (7%), and in four cases (9%) no tumour tissue was found in the material obtained for EM, though found in the material obtained for LM.

Thus, suitable material was available for EM evaluation in 62 out of 76 cases (82%) where tumour cells were detected by LM. These 62 cases were grouped according to the gain in the histopathological specificity of the diagnosis and to its clinical relevance as described in the Material and Methods section. In 23 cases EM was without diagnostic value as the results of the EM examination added nothing to the LM diagnosis. In 12 cases EM provided a more precise histopathological diagnosis compared with LM, for example adenocarcinoma compared with carcinoma, but this diagnostic gain was without clinical significance. Finally, in 27 cases EM was of significant clinical value by providing a more precise diagnosis.

The 27 cases where EM was of significant clinical value could be divided into four groups according to the primary LM evaluation and tumour localisation. The first group included 13 biopsies from the liver or pancreas where the LM appearance was that of moderately to well differentiated small round-cell tumour cells thus giving rise to a suspicion of an endocrine tumour. Examination by EM showed that five of these 13 cases were of endocrine origin as the tumour cells contained large amounts of dense core granules. Six cases were adenocarcinomas without endocrine differentiation while, in two cases, EM demonstrated that the cells originated from normal exocrine pancreas, implying that the LM suspicion of tumour was incorrect. Re-evaluation of the primary LM material in the two latter cases confirmed the EM diagnosis.

The second group was composed of nine biopsies from the liver or retroperitoneal lymph nodes where LM examination showed undifferentiated small-cell tumour. Electron microscopy demonstrated that four of these cases were malignant lymphomas and four were metastases from small-cell carcinoma of the lung, while one was an adenocarcinoma.

The third group was made up of three solitary retroperitoneal tumours in close relation to one of the adrenal glands. Evaluation by LM showed well differentiated small-cell tumour, while EM supplied the more specific diagnosis of paraganglioma in two cases and phaeochromocytoma in one case.

The last group consisted of two miscellaneous cases. In one, EM demonstrated a retroperitoneal tumour to be a sarcoma. The other case was that of a patient who had previously been treated for both adenocarcinoma of the breast and malignant melanoma and who now presented with liver metastases. Light microscopy was unable to distinguish between these two tumour cell types in the sample from the liver metastases, while EM could demonstrate that the tumour cells derived from an adenocarcinoma and that the metastases therefore were from the patient's breast carcinoma. The chemotherapeutic treatment was planned accordingly.

Discussion

The present prospective study has focused on the indications for performing EM on ultrasound-guided fine-needle biopsy specimens and the possible clinical advantages of the method Two methods of obtaining material for EM, namely by fine-needle aspiration and by fine-needle histological biopsy (Surecut), were tested. The yield of material suitable for EM examinations was similar in both methods, namely 24 out of 31 cases (77%) by aspiration and 38 out of 45 (84%) by Surecut biopsy. However, the Surecut method is technically easier to use as centrifugation is unnecessary and the fragments of tumour tissue which are available for ultrathin sectioning tend to be larger.

The value of EM in tumour histopathology is that it enables the determination of the histogenesis of the tumour cells in question (Ghadially, 1980; Henderson & Papadimitriou, 1982). As the great majority of abdominal tumours and retroperitoneal metastases are adenocarcinomas, EM will be of no value in these cases as it will only confirm what is apparent by use of routine LM. However, in instances of tumours which are undifferentiated by LM, especially in undifferentiated small-cell tumours, EM is often able to distinguish between the clinically important diagnoses of small-cell carcinoma of the lung, malignant lymphoma, sarcoma and endocrine tumour. This was confirmed in the present study, as the clinical gain from employing EM as an additional investigative procedure was of significance in 27 of the 76 cases (36%) where tumour was suspected by the standard LM examination and in 27 of the 62 cases (44%) where material suitable for EM examination was obtained.

During the 3-year period of the investigation, the department of ultrasound performed 899 fine-needle biopsies on suspected intra-abdominal or retroperitoneal tumours. This demonstrates that, even when the rather wide indications employed in the present study are used, EM examination is indicated in only approximately 10% of all fine-needle biopsies from these sites. By narrowing these indications, it is conceivable that the rate of clinically significant information obtained by EM would be raised. On the other hand, it is simple to discard the extra sample obtained for EM when LM is conclusive. The extra biopsy only prolongs the ultrasound investigation by the time for one additional pass with the fine needle and the extra inconvenience to the patient may be regarded as minimal compared with the possible extra gain of clinically important diagnostic information. The present study has shown conclusively that EM examination can be of significant importance in the correct handling of the investigative procedure and treatment of the patient in question.

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Book reviews

Ultrasound Annual 1986. Ed. by Roger C. Sanders and Michael C. Hill, pp. x+270, 1986 (Raven Press, New York), $87.00. ISBN 0-88167-241-6

As in previous years, this annual presents useful review articles on fields where there have been recent developments in ultrasound. In addition, there are two more general chapters this year: one on malpractice and ultrasound, outlining possible pitfalls or errors which could potentially lead to legal action, and the other on department design. These are both of more relevance to American than to British radiologists, unfortunately so in the latter case, as the design of the Johns Hopkins ultrasound department as described is beyond the wildest dreams of any NHS consultant.

There are two excellent chapters on paediatric ultrasound covering the gastrointestinal tract (including useful normal values for pancreas, bile ducts etc.) and antenatal ultrasound of the genitourinary system. Both give clear, concise accounts of the current state of the art with good illustrations and up-to-date references. The chapter on ovarian follicle retrieval for IVF gives a good account of the various techniques available and there is a rather long, but reasonably comprehensive, chapter on Doppler ultrasound in obstetrics.

The account of endoscopic ultrasound was disappointing as too much space was devoted to the development of endoscopic probes with only a limited discussion of its clinical applications, principally confined to the upper abdomen. The "throat ultrasound" section discusses the detection of cervical lymphadenopathy, the salivary glands and other cysts and masses encountered in the neck excluding the thyroid and parathyroid. No new developments are described, but an extensive bibliography is provided. The remaining chapter, on benign scrotal disease, provides a good review of the subject, but is the only chapter where the illustrations, although adequate, are of suboptimal quality.

As with all multiauthor books, there is some fluctuation in quality and, in general, I think this year's volume does not reach quite as high a standard as its recent predecessors. This is a useful book, however, for radiologists with an interest in ultrasound and would make a worthwhile addition to a departmental library.

F. E. WHITE

Quantitative Obstetrical Ultrasonography. By R. L. Deter, R. B. Harrist, J. C. Birnholz and F. P. Hadlock, pp. viii+377, 1986 (John Wiley & Sons, New York), £43.25
ISBN 0-471799947

The meat of this book is in the first half. This section is essentially a monograph on the published data relating to fetal and uterine growth, dating of the pregnancy, fetal-weight estimates and abnormalities of fetal growth. Comparisons are made of the published data, and there are analyses of the subjects, accuracy of and difference in the various studies. Most of the parameters of head size, the trunk and long bones are discussed; renal size is not analysed. There is a chapter on fetal dynamics, eye and eyelid movements, fetal breathing movements, blood flow measurements and bladder filling, and this section is more concise.

The next section, taking up a third of the book, is a basic introduction to statistics, with very little specific reference to obstetrics and it seems out of place in this book.

Finally there are substantial appendices tabulating the published data on fetal and obstetric measurements, with reference, for instance, to the population studies, technique of measurement, the method of data analysis, and the effectiveness in identifying abnormal growth.

All this is pretty turgid reading, made more difficult by the very widespread use of initials, both in the text and in the tables. Anyone contemplating publishing on the subject of fetal growth or well-being will find the compilations of earlier papers invaluable. Most of the authors of this book, and others, have contributed to conventional textbooks of obstetrical ultrasound and the average reader would prefer these more general reviews.

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The relationship between the bladder and the cervix in patients undergoing intracavitary therapy

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ABSTRACT

Previous studies have shown a poor correlation between bladder damage and bladder dosage in patients treated with radiation therapy, including intracavitary therapy for uterine tumours. This study was undertaken to investigate prospectively the relationship between the cervical os and the bladder in patients undergoing intracavitary treatment. The computed tomography scans of 59 patients undergoing intracavitary treatment were analysed. The upper limit of the undistended bladder relative to the os extended from 5.5 cm cephalic to the cervix to 4.0 cm below it. The distance from the central tube to the posterior bladder wall at the level of the cervix ranged from 1.5 cm to 4.2 cm. This was positively associated with size of ovoid ($p = 0.022$), though with considerable individual variation. A separate analysis failed to show a consistent correlation with age or stage of disease. Thirty-nine of the 59 patients (65.5%) had asymmetrical bladders. Of these, half had "slight" asymmetry and the others had "marked" asymmetry. The thickness of the vesico-vaginal septum varied from 0.5 cm to 2.9 cm but was difficult to assess in some patients. In patients treated with medium-sized ovoids and those with Stage IB and IIB disease, the distance to the bladder base is greatest, though there is marked individual variation. These investigations reveal a marked variation in bladder position relative to the cervix in patients undergoing intracavitary therapy. The position of the bladder cannot be accurately predicted by any of these clinical criteria and requires to be defined by a radiological technique in the individual patient.

Radiation-induced bladder-base damage is a well recognised potential complication of intracavitary therapy for patients treated radically for carcinoma of the cervix (Kottmeier & Gray, 1961; Perez et al, 1984). Unfortunately, clinical studies have failed to show a consistent relationship between bladder doses, measured or calculated, and late radiation damage. In a recent publication the International Commission on Radiation Units and Measurements (ICRU) (1985) has proposed a reference point for expressing bladder-base dosage. However, a previous study at this institute (Hunter et al, 1986) has shown no correlation between this reference-point dosage and the maximum bladder-base dosage calculated using data from computed tomography (CT) cross-sectional images. Some authors have suggested that "other factors", including differences in pelvic anatomy, have a part to play.

The present study was undertaken to investigate prospectively the relationship between the cervical os and the bladder in patients undergoing intracavitary treatment in an attempt to identify any relationship between the cervix and the bladder position, the distance to the bladder base and bladder symmetry.

MATERIALS AND METHOD

Patients

The study group consisted of 59 patients with carcinoma of the uterus. Of these patients, 55 had carcinoma of the cervix and four patients were treated for carcinoma of the body of the uterus. Among those treated for carcinoma of the cervix, 33 patients were found to have early-stage disease (Stage I or IIA) and 22 patients had Stage IIB or III disease. All patients were being treated by intracavitary therapy using the Selectron low dose-rate remote afterloading system (Nucletron Trading) with standard Manchester-style Selectron applicators as primary treatment or in association with external beam therapy.

All the CT scans used in this investigation were taken on an EMI7070 whole-body scanner during routine radiotherapy sessions. Patients were scanned supine, in their treatment position, with 20 ml of Urografin-based contrast medium (Schering AG) and 20 ml of air instilled into the bladder via an indwelling catheter. The scanning technique provided antero-posterior and lateral digital scan projection radiographs and a series of intersecting cross-sectional scans. An initial cross-sectional image was taken through the base of the ovoids, as identified from the lateral view of the patient. Subsequent sections were taken at 0.5 cm intervals until only the central applicator was visible. Scanning was then continued at 1 cm intervals until the applicators were cleared. The images were then archived to floppy disc for analysis using a Data General S130 minicomputer, normally used for treatment planning.

Technical description

A range of programs (Wilkinson et al, 1983) had already been written to enable visualisation of selected dose-rate points and contours on CT scans of patients undergoing intracavitary treatment. These were expanded to improve viewing and archiving facilities so enabling easy review of accumulated studies. In particular, tracker-ball controlled screen ruler was implemented using the colour facilities available on the image display monitor. This allowed the gathering of data on the relative orientations and dimensions of anatomical features. As an aid to accurate positioning, the ruler operated under an image magnification of ×1, ×2 or ×4. As the operator

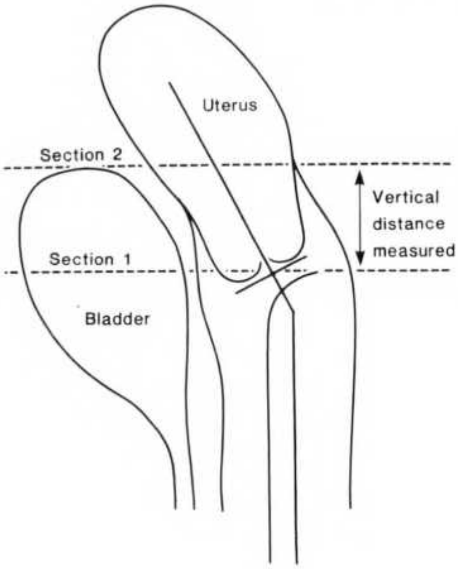


FIG. 1.

Schematic diagram showing how upper limit of bladder was assessed relative to the cervix.

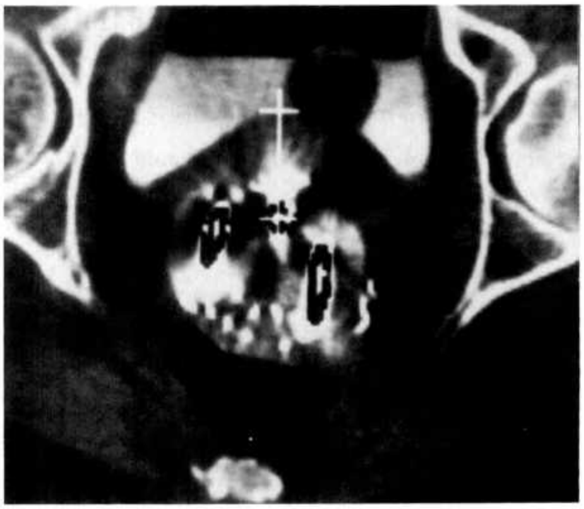


FIG. 2.

CT scan to show how the minimum distance from central tube to bladder base was measured.

altered the ruler position, dimension and orientation, a continuous display of these parameters was maintained on the keyboard display unit. In addition, simple image enhancement was found to be extremely effective in revealing important detail in lateral images of consistently poor quality. It particularly accelerated the acquisition of knowledge concerning the relative orientation of applicators and key anatomical features such as the sacrum (Moore, 1985).

Measurements

Upper limit of bladder. On looking at the serial sections obtained, the most cranial section through the ovoids was identified. The cervix was identified on the next section. The most cranial section through the bladder was identified by visualising the section where the contrast medium was still visible in the bladder. The vertical distance between these serial sections was measured and gave the height of the top of the bladder relative to the cervix. Figure 1 shows schematically how this was achieved in practice.

Distance of the central tube to the posterior wall of the bladder at the level of the cervix. The minimum distance from the central tube to the posterior wall of the bladder was measured at the level of the cervix using the method shown in Fig. 2. In 13 patients the level of the bladder did not extend to the cervix. The distance in nine of these 13 patients was measured at 0.5 cm or 1.0 cm below the cervix, depending on the upper limit of the bladder.

Symmetry of bladder. The symmetry of the bladder in relation to the cervix, vaginal applicators and central tube was assessed. This was done by measuring the distance from the central tube to the most posterior extent of the bladder (round the vagina) as shown in Fig. 3.

Vesico-vaginal septum. The minimum thickness of the vesico-vaginal septum was measured as shown in Fig. 4. The measurement was undertaken at a level just below the level of the cervix.

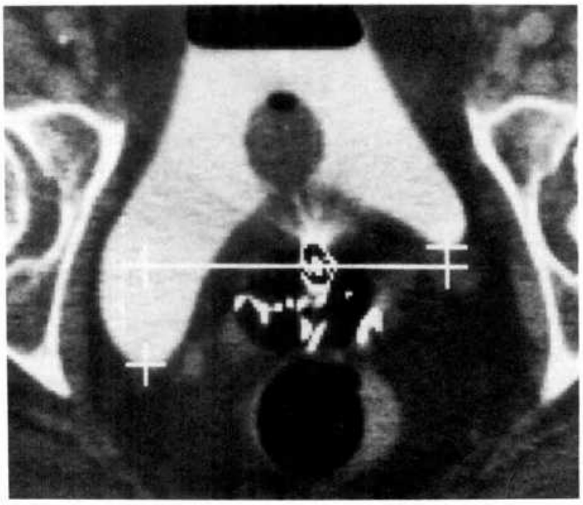


FIG. 3.

CT scan showing how degree of bladder asymmetry was assessed.

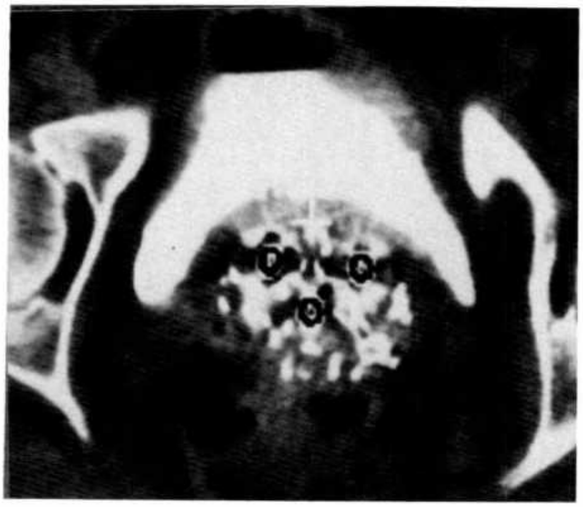


FIG. 4.

CT scan showing how minimum vesico-vaginal thickness was assessed.

RESULTS

Upper limit of the undistended bladder

Figure 5 shows a histogram of the distribution of the upper level of the bladder relative to the cervix. In the majority of the patients, 39 out of 59 (66%), the upper limit of the bladder was within ±1 cm of the level of the cervix. However, the upper limit of the bladder varied from 5.5 cm above the cervix to 4.0 cm below. In two patients the upper limit could not be assessed because of technical difficulties.

Distance from central tube to posterior bladder wall

The histogram in Fig. 6 shows the variation in distance between the central tube and posterior bladder wall at the level of the cervix. The distance measured ranged from 1.5 cm to 4.2 cm, mean value 2.77 cm. In the majority of patients, 43 out of 55 (78%), the distance measured was in the range of 1.9 cm to 3.4 cm. In four patients it was not possible to measure this distance for technical reasons. The scatter diagram (Fig. 7A) shows the relation between this distance and age. An inverse relationship was observed which was of borderline significance ($p = 0.067$). A separate analysis was undertaken to investigate the relationship between the distance from the central tube to the posterior bladder wall and stage of disease (Fig. 7B): there was poor correlation ($p = 0.103$). There was a trend for this distance to be greater in patients with Stage IB and IIB disease compared with Stage IA and IIA disease. This distance was also significantly higher in patients where medium-sized ovoids (Fig. 7C) were used compared with smaller ovoids ($p = 0.022$). Despite these observations, marked individual variation was noted.

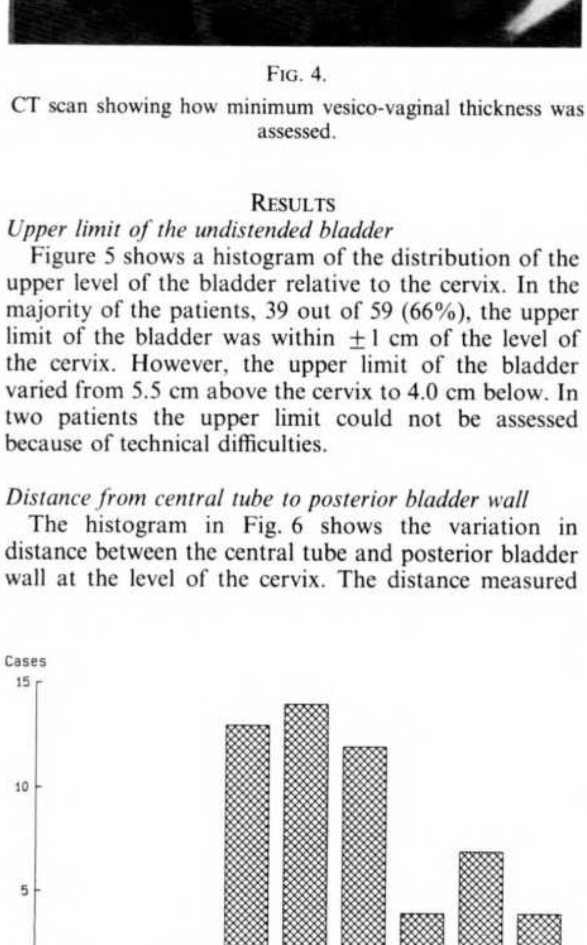


FIG. 5.

Distribution of distances from cervix to upper limit of bladder (57 cases).

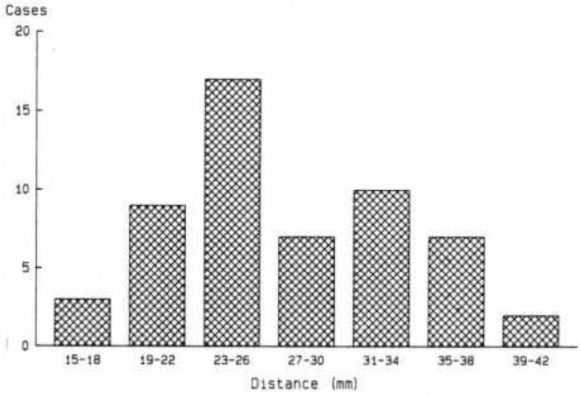


FIG. 6.

Variation in distance from central tube to posterior bladder wall (55 cases, four not assessable).

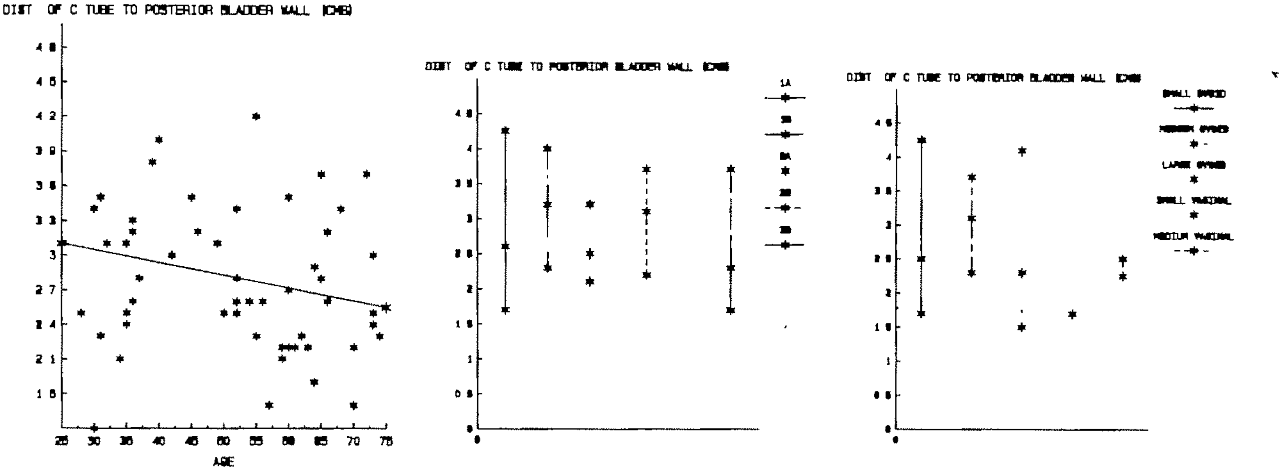
Symmetry/asymmetry of bladder

Of the 55 patients for whom it was possible to comment on the symmetry of the bladder, only 19 patients (34.5%) were found to have a bladder which was symmetrical about the vagina: in 36 (65.5%) it was asymmetrical (Table I). In four patients it was not possible to comment on this feature. The asymmetry was defined as being "slight" where the difference in

TABLE I

SYMMETRY/ASYMMETRY OF BLADDER IN 59 CASES

	Cases	% of 55 cases assessed
Symmetrical	19	34.5%
Asymmetrical	36	65.5%
slight	19	
marked	17	
Impossible to assess	4	



A B C

FIG 7.

Scatter diagrams of (A) distance from central tube to posterior bladder wall and age, (B) distance from central tube to posterior bladder wall and stage of disease, and (C) distance of central tube to posterior bladder wall and size of ovoid.

posterior extents of the bladder on either side of the cervix was less than 2 cm and "markedly" asymmetrical where this difference was greater than 2 cm. Figure 3 shows how this was assessed. In those patients with asymmetrical bladders the asymmetry was classed as being "slight" in 52.8% (19 out of 36 patients) and as "marked" in 17 patients (47.2%).

Vesico-vaginal septum

The thickness of the vesico-vaginal septum at the level of the cervix varied from 0.5 cm to 2.9 cm, mean value 1.29 cm. Figure 8 shows the frequency distribution. In 23 patients the thickness could not be measured accurately owing to radiological difficulties in identifying the septum or failure of the bladder to extend to the level of the cervix.

DISCUSSION

Several clinical studies have been undertaken to assess bladder dosage during intracavitary therapy. Methods that have been used include scintillation probes (Fletcher et al, 1958), LiF rods in catheters (Kivinitty et al, 1971) and portable ionisation probes (Million et al, 1966). Attempts to correlate bladder damage with measured bladder dose have shown a poor relationship (Fletcher et al, 1958; Peckham et al, 1969). The former of these studies concluded that this correlation showed "a great margin for tolerance". Other studies have attempted to correlate bladder doses obtained by calculation (Peckham et al, 1969), with actual measurements (Nieminen et al, 1970). Despite this lack of correlation, a reference point on the posterior bladder wall, as suggested by Chassagne and Horiot (1977), has been incorporated into the ICRU (1985) recommendations on pelvic dosimetry. No data have been provided to support the clinical significance of such a point, particularly with regard to late bladder damage.

Several authors (Fletcher et al, 1958; Million et al, 1966; Cunningham et al, 1981; Hunter et al, 1986) have suggested that other factors may have a part to play. Such factors include variation in size and position of the bladder in relation to the cervix, bladder asymmetry, varying areas of bladder wall receiving a high dose, the inherent inhomogeneity of intracavitary therapy and the extent of disease. When considering bladder dosimetry for intracavitary therapy, the inverse square law plays a very important part and small changes of distance make large differences in dosage.

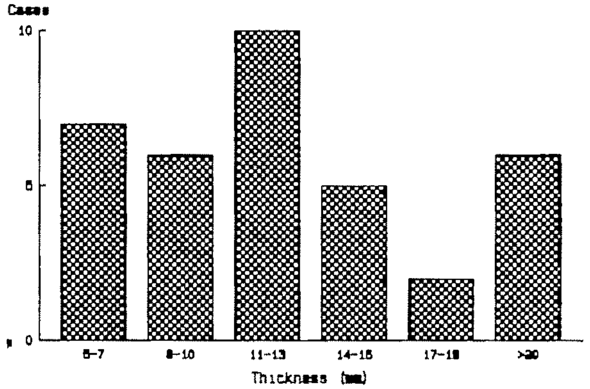


FIG. 8

Variation in vesico-vaginal thickness, (36 cases, 23 not assessable).

The present study involved measurements on the undistended bladder with only a small amount of contrast medium (20 ml) being introduced to visualise the posterior bladder wall. In practice the bladder is left on free drainage during treatment. A wide variation in distance from the central tube to the posterior bladder wall was identified, which is in keeping with the observation of a marked variation in measured or calculated bladder doses in patients. Correlation with clinical parameters has shown the distance to be greatest in patients with Stage IIB disease and those treated with medium-sized ovoids. This distance also correlated inversely with age. Despite these observations there was a considerable degree of individual variation, making prediction of this distance in the individual patient impossible.

The investigation has also shown a considerable variation in bladder position and symmetry relative to the cervix and applicators. The area of the bladder wall receiving a high dose would, as a result, be expected to vary considerably from patient to patient. This factor has so far been ignored when considering bladder damage and yet might be expected to influence tolerance.

Despite this lack of correlation, accurate calculation of the dose to the posterior bladder wall could alert the radiotherapist to patients at risk from bladder damage. A previous study at this hospital (Hunter et al, 1986) has shown an unfortunate lack of correlation between maximum bladder-base dose and the dose received at the reference point as defined by the ICRU. Better correlation was observed between a point on the posterior bladder wall in a plane vertical to the vaginal sources. The present study shows that the bladder extends to the level of the cervix in the majority of cases and doses can be calculated in this region provided the real distance from the base of the bladder to the sources is known. The marked individual variation makes prediction of bladder position by clinical criteria impossible. The position of the bladder in relation to the applicators and sources has to be positively defined in the individual patient if patients at risk of damage are to be identified.

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Book review

Radioactive Waste Proceedings of the 21st Annual Meeting of the NCRP, 3–4 April 1985. National Council on Radiation Protection and Measurements. pp. iii+289, 1986 (NCRP, Bethesda), $20.00.
ISBN 0–913392–81–2

This volume is an account of the proceedings of the 21st Annual Meeting of the NCRP, and includes the text of the 9th L. S. Taylor lecture, given by John H Harley.

While the proceedings contain some points of general interest, the papers are very much geared to the American scene, with copious reference to their various programmes for waste disposal and the welter of regulations and legislation which is becoming increasingly associated with them. Being a National Council, the American orientation is expected, but it inevitably limits the wider appeal which is usually a characteristic of NCRP proceedings.

The scientific session contains 15 papers devoted to the main topic, "radioactive waste". It begins with a survey of quantities and sources of radioactive waste in the USA. This is followed by a lecture on considerations of the *de minimis* concept and exempt quantities which stresses the need for the establishment of a negligible risk level (NRL) which would produce economic benefit in many areas, eliminating such things as "expensive, futile epidemiological studies at very low exposure levels". This aspect is taken up by a number of other lecturers in later chapters. Extreme low-level requirements frequently get into regulations and legislation, leading to ridiculous situations. Some very amusing and pertinent examples are given in the paper by Rosalyn Yalow who, testifying before a Congressional Subcommittee, pointed out that the adult body, with its *natural* burden of 0.1 μCi of ^{40}K and 0.1 μCi of ^{14}C precluded it from burial, incineration or garbage disposal under the then current NRC rules on low-level radioactivity disposal!

Methods of processing low- and high-level wastes are dealt with in several lectures, and details are given of the current construction status of the waste isolation pilot plant in New Mexico and of the US sea-bed disposal programme.

One of the many problems associated with land disposal is the ultimate contamination of the environment that could occur consequent upon erosion of ground-water leaching. Merill Eisenbud and his colleagues describe some work being carried out at a special site in Brazil where a very localised ore deposit, rich in thorium and rare earths, occurs in the side of an isolated hill. Since many of the chemicals present in the deposit simulate in their behaviour the important transuranic actinide elements, detailed geological and hydrological surveys can be used to predict and test the natural movements of such substances in the environment, and the data fed back into schemes for containment and selection of dumping grounds.

Another group of papers is devoted to the scientific basis for disposal of hazardous waste and the handling of specialised materials and mixed wastes. The section closes with a lecture on the particular problem posed by spent reactor fuels.

The Taylor lecture ("Truth (and Beauty) in Radiation Measurement") is a historical survey of progress and refinements in the accurate measurement of small quantities of radioisotopes and contains many anecdotes from the lecturer's wide and varied experience. The main message to come across is the need, in the face of very variable interlaboratory results, for a reliable quality assessment scheme so that valid comparisons can be made.

The proceedings close with a Scientific Briefing Session on regulatory aspects of radioactive waste disposal, again principally relevant to the USA. There are also some reports from a number of NCRP Committees.

Overall, I did not find this volume as enjoyable and informative as the previous ones I have reviewed. This is a very specialised, yet important, topic with a large literature. The inevitable American emphasis certainly limits its usefulness for British readers who might turn to such a volume when looking for a current update review on the subject It is a book for the specialist who wants to know what is going on across the water.

J. R. K. SAVAGE

1987, *The British Journal of Radiology*, *60*, 361–367 APRIL 1987

On-line measurement of field placement errors in external beam radiotherapy

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ABSTRACT

An on-line electronic portal imaging system was used in a quantitative measurement of field placement errors in external beam radiotherapy. Data from 30 patients, giving a total of 150 portals with 66% in the thoracic region and 34% in the abdominal region, were analysed. Displacements from the prescription delineated by physicians were measured. The displacements included errors due to block malposition, field malposition, field malrotation and patient malposition, and these were classified in two categories of displacements, those associated with the portal boundary and those with anatomic structures. Except for one rotational error, only translational errors were found. Displacements greater than 1 cm amounted to 17% with respect to the portal boundary and between 10% and 46% with respect to anatomic landmarks within the portal. From the results of the study, a margin of 1 cm around the tumour is barely sufficient if a 5% accuracy in dose delivery is desired.

In an earlier paper, an on-line electronic portal imaging system has been described (Lam et al, 1986). The initial evaluation of the system showed that the image obtained had adequate contrast resolution for bony structures and air and lung cavities within the portal to be identified. The image data obtained with the system contained precise positional information and were stored in digital form in a computer. By comparing the digital portal image with the digitised image of the simulation radiograph, field placement errors of the treatment portal could be determined. In the work described in this paper the system was used to study the accuracy of the routine patient set-up during the course of the external beam radiation therapy. A quantitative measurement of displacements of the portal boundary from the field boundary drawn by physicians and of some distinct anatomic landmarks in the portal image from those in the simulation radiograph was made. A rather high number of misalignments was found. One possible explanation for this high rate of mismatch could be that some external skin marks might be too variable to serve as field markers and in addition some bony structures might move with respect to others.

METHODS

The imaging system used in this investigation consisted of a microcomputer which moved a linear array of 255 silicon diodes to scan the radiation transmitted through the patient during treatment and processed the collected data to generate an image on a video monitor (Lam et al, 1986). The diode assembly was mounted on a rolling cart which could be placed under the treatment couch in a reproducible position with respect to the centre of the radiation beam by aligning two dowels on the cart with their corresponding holes in the ground. The time required to gather the data for generating the image ranged from about one half of the treatment time to the full treatment time, depending on the prescribed dose for the field and the length of the field to be scanned.

All patients in this study were irradiated with the photon beam of a Varian Clinac 4/100 linear accelerator. Because the diode array was mounted on a cart, only portals obtained with the beam directed vertically downwards were recorded and then analysed. A total of 150 images from 30 patients with various portal shapes were studied. Of the 150 portals, 66% belonged to the thoracic region and 34% belonged to the abdominal region. The patients were set up under the normal routine procedure, such as taking portal radiographs once a week and using skin marks to align the treatment field. Since minimum interference with the routine set-up was desired, the only additional work for the operators involved rolling the cart into position after the patient was set up, and removing the cart at the end of the treatment. The additional time for the operation was about 1 min. No patient adjustment was made based on the information obtained from the on-line portal imaging system.

For this analysis, the correct patient set-up was based on the prescribed field size and shielding blocks delineated by physicians on the simulation radiograph obtained from the Oldelft Simulix simulator. These markings together with distinct anatomic landmarks, such as bones, air and lung cavities, were digitised by an XY-digitising tablet into the data analysis computer as outlines (Lam et al, 1986). From the recorded focus-to-film distance the outlines were scaled so that they had the same magnification as that of the portal image. The outlines were displayed on an overlay plane of the graphics system. Figure 1 shows an example of a portal image together with the digitised outlines. The outlines

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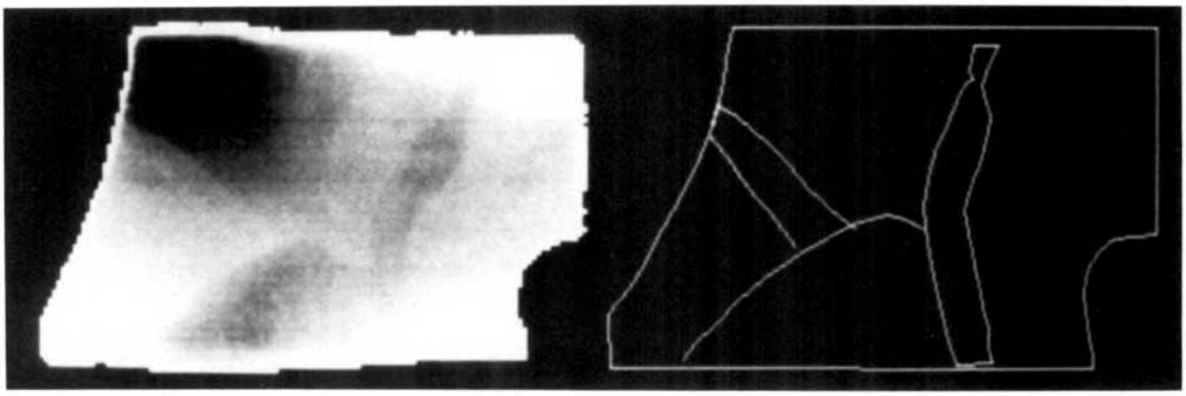

FIG. 1.

Portal image and digitised outlines. (A) Image of the upper thorax obtained from the electronic portal imaging system. (B) Outlines digitised from the simulation radiograph.

could be shifted and rotated with respect to the portal image by means of interactive graphics.

Two general types of errors were analysed.

(1) Portal boundary

The first step in determining field placement errors involved moving the digitised outlines until the field boundary from the simulation radiograph matched as closely as possible with the portal image. Figure 2 illustrates the results of shifting the digitised outlines in Fig. 1 to obtain an optimum matching of the field boundaries. The origin of the digitised outlines in "pixel co-ordinates" was then recorded and used as the reference point. To determine the extent of the misalignment, the outlines were shifted until the required alignment with a particular structure was obtained. The co-ordinates of the new origin were read and the displacement in pixels was determined. Each pixel corresponded to 0.67 mm when projected to the mid-coronal plane of the patient at the isocentric distance from the source of the therapy machine. Misalignment might occur at several positions. It can be seen in Fig. 2 that this occurred at both the upper left-hand corner and lower right-hand corner of the portal. The digitised outline was then moved to match different segments of the boundary of the portal image and the displacement in each case was recorded. Only the maximum deviation was considered in this analysis.

(2) Anatomic structures

After an optimum alignment of the portal boundaries was achieved, each of the several digitised lines was

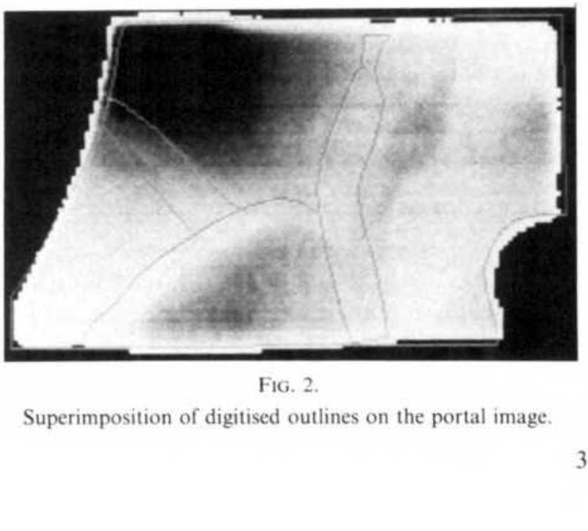

FIG. 2.

Superimposition of digitised outlines on the portal image.

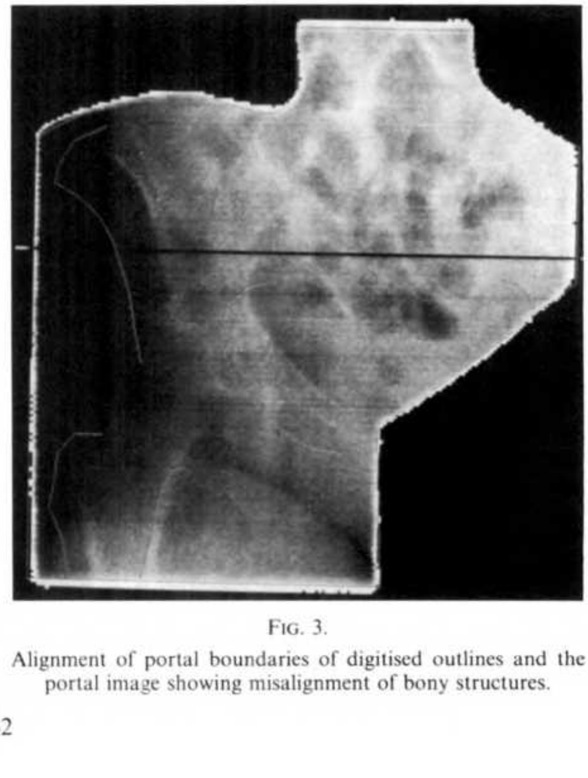

FIG. 3.

Alignment of portal boundaries of digitised outlines and the portal image showing misalignment of bony structures.

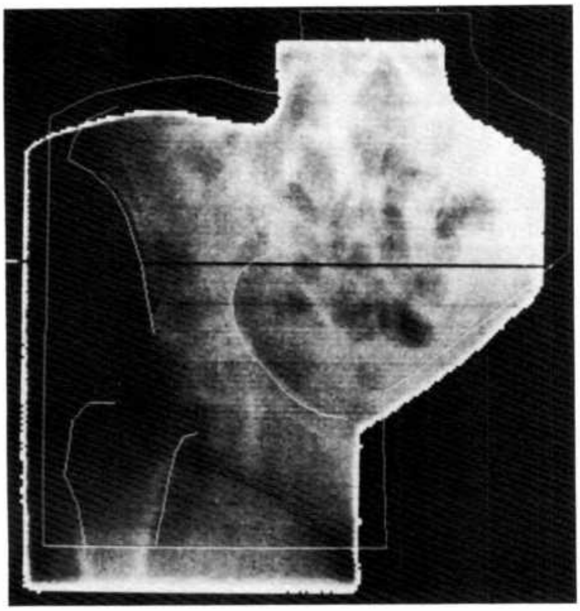

FIG. 4.
Displacement of the digitised outlines to achieve an alignment of the bony structures.

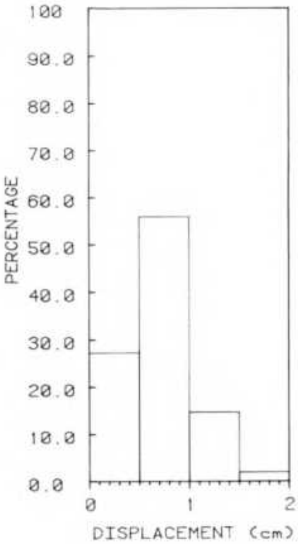

FIG. 5.
Frequency distribution of displacements in radiation portal boundaries. The bin for 1.5–2.0 cm includes displacements greater than 2.0 cm.

shifted in turn to obtain an exact match with its corresponding anatomic structure. The displacement in each case was recorded. Figure 3 shows an example of the alignment of the portal boundaries, and Fig. 4 demonstrates the corresponding alignment of the bony structures. It was possible that different structures might require different displacements in order to get an exact alignment.

RESULTS

In the 150 portals studied here, most of the errors detected were translational errors. Rotational errors were usually small, except in one case where the field length and width were interchanged. Magnification errors in all cases were less than 2%, which was within limits expected of the simulator and therapy machine specifications.

In the study of field boundary errors, only the maximum discrepancy in each portal was considered since any discrepancy must be regarded as an error. Figure 5 shows the frequency distribution of displacements with respect to the portal boundary. Misalignments greater than 2.0 cm are included in the interval 1.5–2.0 cm. It can be seen that of 150 portals, 41 (27%) were within 0.5 cm of the prescription and that 125 (83%) agreed to within 1.0 cm of the prescription.

In the analysis of alignment errors associated with anatomic sites, it was expected that a range of values of misalignment would be possible. In the same portal the digitised outlines of different anatomic structures might have to be moved different distances to achieve an exact alignment. For each portal, the structure which had the minimum displacement was chosen to give the most optimistic estimation of the misalignment error, whereas the maximum displacement was taken as the most pessimistic estimation of the error. The frequency distribution of minimum displacements in the localisation of anatomic structures with respect to the portal images is shown in Fig. 6, where the range 1.5–2.0 cm also includes cases with misalignments greater than 2.0 cm. As can be seen in the histogram, by the most optimistic estimation, 15 (10%) of the portals had displacements of 1.0 cm or more. Figure 7 shows the corresponding frequency of maximum displacements. Here five cases with more than 2.0 cm displacement are put in the bin for 1.5–2.0 cm. The results indicate that

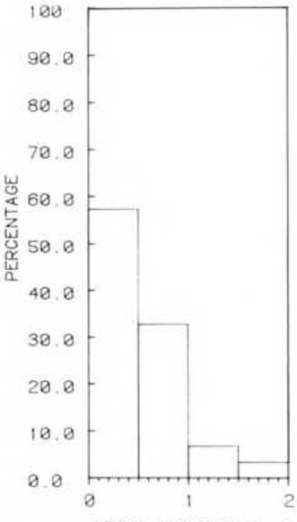

FIG. 6.
Frequency distribution of minimum displacements in the localisation of anatomic structures. The bin for 1.5–2.0 cm includes displacements greater than 2.0 cm.

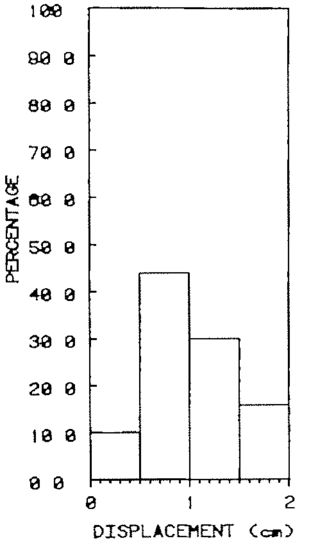

Fig 7

Frequency distribution of maximum displacements in the localisation of anatomic structures The bin for 1.5–2.0 cm includes displacements greater than 2.0 cm.

in the worst possible situation 69 (46%) of the portals had misalignments of more than 1.0 cm.

Discussion

The high cost of using computed tomography (CT) scanners in radiation therapy has been justified by a cost–benefit analysis based mainly on improvements in treatment plans (Goitein, 1980). However, those improvements would only be of academic value unless the precision of radiation delivery matches the accuracy of the generated plans. The present study is the first attempt to use an on-line electronic imaging system to monitor field placement errors in radiation delivery. All data were represented in digital form, suitable for analysis in a computer. Since images had the same magnification, precise quantitative measurement was possible by using interactive graphics to compare portal images with digitised outlines from simulation radiographs directly. Moreover, in a graphics overlay of two images, any mismatch would show up clearly.

Some previous studies have been carried out to determine field placement errors by using verification radiographs (see, for example, Marks et al, 1974, 1976; Byhardt et al, 1978) and to record errors in setting the parameters of the therapy machine (Kartha et al, 1975). However, the quantitative measurement of errors by comparing a verification radiograph with a simulation radiograph of a different magnification is a laborious process which requires a large amount of manual effort to produce accurate results. Since the facility of direct comparison was not available to investigators of previous studies, some of the discrepancies reported here might have been missed because they were difficult to detect in a visual comparison of two radiographic images of different magnifications.

The portal should match exactly with the prescription which defined the target volume to be irradiated and the normal tissues or vital organs to be protected. Any deviation from the prescription must be considered as an error. The seriousness of the error is a clinical judgment for the physician in charge. Misalignment in the portal boundary, such as that shown in Fig. 2, was mainly caused by incorrect setting of the collimator field size and/or the incorrect cutting and mounting of the shielding blocks.

Displacements, which ranged from 10% to 49% found in this study for a margin of 1.0 cm, seemed to be high. One possible explanation for this high misalignment rate could be that the skin and subcutaneous tissues might have moved with respect to the underlying musculature and skeleton, causing the external field markers to shift in reference to the internal anatomy, and in addition some bony structures might have moved relative to some others from one set-up to another. However, the displacements reported here were not substantially higher than those obtained by Byhardt et al (1978) for the trunk region. As Byhardt et al have noted, the errors detected by using weekly localisation radiographs might not reflect field placement variations that occurred on a daily basis.

Currently the clinical determination of the acceptability of the field placement precision is based on visual comparison of the portal radiograph with the simulation radiograph. The anatomic structures chosen for comparison are rather subjective, as some structures are considered too fluid to be taken into consideration. The degree of seriousness of a particular discrepancy is judged according to the anatomic site. In this analysis, however, all distinct anatomic landmarks were considered. Some of the shifts in the bony structures could be because of a slight change in the posture of the patient lying on the couch, while others might have been because of the weight changes of the patient during the course of the treatment.

One conclusion that can be drawn from this investigation is that skin marks may change in relation to the internal anatomy. Also, some anatomic structures can shift from one set-up to another. The same can be said about the tumour since the movement of one structure could affect the location of another. Hence in marking the target volume, the possibility of the tumour shifting should be taken into consideration by having an appropriate margin around it. If a 5% accuracy in dose delivery is required for all parts of the tumour volume, then a margin of 1 cm is hardly sufficient from the observation of this study.

Some improvements on the portal imaging system are possible. For example, an on-line monitoring system that can generate an image with a small dosage of radiation and automatically recall the digitised outlines from the simulation radiograph to superimpose on the portal image will be helpful in improving the precision of radiation delivery. It can correct such accidental errors as the field length and width being mistakenly interchanged or the focused block tray not being put in place properly. Patient adjustment can also be made if it is found necessary before the full dose is given. However, because of the high probability of the movement of the tumour with respect to skin marks, the time-consuming procedure of frequent patient re-adjustment may be too burdensome for the operators. In order for such a monitoring system to be useful, it has to be associated with a remote control of the patient support assembly so that some adjustments can be performed from the control console of the therapy machine.

ACKNOWLEDGMENTS

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The co-operation of the technologists operating the Clinac 4/100 in acquiring portal image data of patients is gratefully acknowledged.

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Book review

An Introduction to Radiation Protection. 3rd edn. By A. Martin and S. A. Harbison, pp xi+247, 1986 (Chapman and Hall, London), £7.95 paperback, £15.00 hardback.
ISBN 0-412-27810-3 (paperback)
0-412-27800-6 (hardback)

This is the third edition of this useful and very readable book, revised and updated to take account of advances in technology and changes in safety regulations and requirements It contains 17 chapters, each broken up into a number of short subsections, reviewing the important points with minimum "padding". The headings have been carefully planned and printed with adequate spacing so that one can quickly find one's way around the book without continual recourse to the index.

The first three chapters ("The structure of matter", "Radioactivity and radiation" and "Radiation units") concentrate on the basic physics Chapter 4 is a short introduction to some of the principal biological effects of radiation. Chapter 5 considers natural and man-made radiations, providing information about the relative population exposures from the various sources Chapter 6, on the system of dose limitation, introduces the work and recommendations of the ICRP, in particular their Publication 26 and its extensions I found this section most helpful, the authors have presented a clear summary without delving too deeply into the underlying philosophy. The next few chapters (7-13) turn to applied radiation protection. After outlining the various methods for detecting and measuring radiation (Chapter 7), the situations arising from external radiation (Chapter 8) and internal radiation (Chapter 9) are compared and contrasted Simple, worked examples of calculations which may come the way of a radiation safety officer are provided throughout, covering such topics as "shielding" and "annual limits of intake". The particular problems posed by nuclear reactors and radioactive waste disposal form the subjects for Chapters 10 and 11, while Chapters 12 and 13 lead into the more specialised problems associated with the ever-increasing medical uses of radiation and radionuclides for both diagnosis and therapy.

The increasing pressure for legally enforceable safety standards and the Health and Safety at Work Act provide material for Chapter 14 and, here again, the authors are to be congratulated on producing some very concise and understandable paragraphs from this extremely complicated area

The last three chapters deal with day-to-day health physics, describing some of the laboratory techniques in common use (Chapter 15), possible radiological emergencies (Chapter 16) and the administrative and organisational requirements of an efficient health-physics service (Chapter 17). A one-page appendix showing the relationships of SI units used in radiation work, a bibliography and an index close the book.

Each chapter concludes with a summary of the salient points that have been covered and some revision questions Answers to numerical problems are also given at the end of the book. Illustrations and graphs are scattered sparingly through the text and are mostly clear and useful.

There is an enormous amount of information packed into a very small space in this volume. This is mostly owing to the ability of these authors to select important issues and express them in clear English. It is an excellent introduction to radiation protection and certainly to be recommended not only to those just entering the field but as a useful reference and revision book for all types of radiation worker—experimentalists included! I shall endeavour to keep my review copy in a handy place

JOHN R. K. SAVAGE

1987, *The British Journal of Radiology*, 60, 367–373 APRIL 1987

The study of human organs by phosphorus-31 topical magnetic resonance spectroscopy

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ABSTRACT

The potential clinical use of topical magnetic resonance spectroscopy (volume selection by static magnetic field gradients) was tested in 50 studies in volunteers Topical magnetic resonance spectroscopy (MRS) was shown to be a straightforward method for localising ^{31}P spectra of brain and liver. However, the spherical shape and fixed position of the selected volume posed serious limitations to the study of heart and transplanted kidney by topical MRS. Phosphorus-31 spectra of $\sim 30\ \mathrm{cm}^{-3}$ of brain or liver could be obtained in 8 min. Ratios of metabolite concentrations could be determined with a coefficient of variation ranging from 10% to 30%. The ratios of phosphocreatine/ATP and inorganic phosphate/ATP in brain were 1.8 and 0.3, respectively. The ratio of inorganic phosphate/ATP in liver was 0.9. Intracellular pH was 7.03 in brain and 7.24 in liver. The T_1 relaxation times of phosphocreatine, inorganic phosphate and γ-ATP in brain were 4.8 s, 2.5 s and 1.0 s, respectively.

Magnetic resonance spectroscopy (MRS) has now been used for many clinical investigations, although largely in the study of human muscle (for a review, see Radda & Taylor, 1985). For the examination of internal organs it is essential to have methods that can give reliable and reproducible localisation within a time limit acceptable to a patient. While in principle there are many different ways of obtaining spectra from a region of interest, several of these are not applicable to the study of humans, either because the necessary hardware is not compatible with the anatomy, or because the experiment takes too long for routine use So far, three principally different techniques have been proposed and verified experimentally on humans for localised spectroscopy. (1) Rotating frame imaging (Styles et al, 1985) and its derivation, Fourier series depth selection (Garwood et al, 1985; Metz & Briggs, 1985; Blackledge et al, 1987), to derive spatial information by encoding position relative to a gradient in the transmitter field. (2) Volume selection by switched magnetic field gradients has been achieved in two different modes (Bottomley et al, 1984; Bottomley, 1985; Ordidge et al, 1986). (3) Magnetic field profiling by static field gradients, also called topical magnetic resonance (Gordon et al, 1980; Hanley & Gordon, 1981), which is the subject of this paper. The method relies on the use of special gradient coils which produce an approximately spherical volume of homogeneous magnetic field in regions close to the centre of the magnet. Outside this region the magnetic field becomes rapidly inhomogeneous. Thus, narrow spectral lines are obtained from tissue situated in the homogeneous zone, but signals from the surrounding tissue are significantly broadened and can be removed from the spectra mathematically by deconvolution. Topical MRS was first applied in animal experiments in 1980 (Gordon et al, 1980) and has recently been used for studies of normal human liver (Oberhaensli et al, 1986a) and metabolic brain disease (Hayes et al, 1985). It is being used in this laboratory as one of our routine techniques in the investigation of a variety of pathological states (Oberhaensli et al, 1986b) and has been applied so far in almost 100 clinical studies. At this stage of the development of clinical MRS, it is essential to establish the disadvantages and limitations of different approaches, and in this paper we report our examination of the reproducibility of topical MRS for studies of brain, liver, heart and transplanted kidney. In addition, measurements of spin lattice relaxation times (T_1) of phosphorylated metabolites in brain are reported

METHODS

A 1.9 T superconducting magnet (Oxford Magnet Technology) with a clear bore of 60 cm was used. The magnet was equipped with a special set of gradient coils (z^4 and z^2 gradients), by which the homogeneous volume (homogeneity 0.1 ppm) of the magnet could be varied between a spherical volume of $\sim$4 cm and $\sim$10 cm in diameter (Hanley & Gordon, 1981).

Data were collected with either a single-turn 8 cm surface coil or, for some brain spectra, a Dadok-type coil which had a diameter of 25 cm and a window length of 14 cm. The surface coil was tuned to both the phosphorus and proton frequencies using a conventional double-tuned circuit as shown in Fig. 1. Hoult (1978) shows that the loss of sensitivity suffered by double tuning is given by:

For ^{1}H. $$\Delta S/N = \left(1+\frac{LQ_{\mathrm{L}}}{MQ_{\mathrm{M}}}\right)^{-\frac{1}{2}}$$

For ^{31}P: $$\Delta S/N = \left(1+\frac{MQ_{\mathrm{L}}}{LQ_{\mathrm{M}}}\right)^{-\frac{1}{2}}$$

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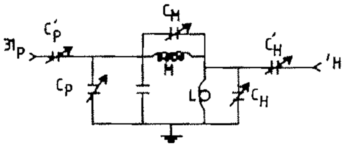

FIG. 1.

Electrical circuit for doubly tuned radiofrequency coil. For details, see text.

where S/N is the signal-to-noise ratio, L is the probe inductance, M the double-tuning inductance and Q_L and Q_M the quality factors of L and M, respectively (measured at the relevant frequency).

At the frequencies of our experiments the Q of the surface coil is dominated by losses in the sample, and so, it is possible to achieve a much higher Q for M than for L. Therefore, in contrast to the conventional wisdom of high-resolution MRS, the circuit can be made to work efficiently at both frequencies. By choosing $M \sim L$, the loss of sensitivity at both frequencies will be only of the order of 10%. The advantage of this system is that the pulse widths for the proton and phosphorus frequencies are comparable, which facilitates shimming. The 90° pulse width at coil centre for ^{31}P was 100 μs using a power of 150 W.

The whole-head coil was tuned to the ^{31}P frequency and, via an impedance transformer, to the proton frequency (Gordon & Timms, 1982). The 90° pulse width for ^{31}P was 500 μs using a power of 150 W.

Data acquisition and analysis

The magnetic field homogeneity was optimised with the diameter of the homogeneous volume set to 10 cm. The homogeneity of the magnetic field was considered acceptable when the line width of the water resonance at half height was 0.5 ppm. Then the diameter of the homogeneous volume was reduced to 4 cm and ^{31}P spectra were collected. Positioning the subject and shimming the magnet took about 10 min. The spectra were deconvoluted using the function

$$P(t) = \frac{1}{1 + n \exp(-t/T_2')}$$

where n is the ratio of the signal intensity from the broad components to the signal intensity from the narrow components and T_2' is the time constant for the broadening contribution of the profiled field (Gordon et al, 1982). The value for T_2' was determined by measuring the line width of the broad resonance in the non-deconvoluted spectrum. Then, by inspection of the free induction decay, a value for n was determined so that the envelope of the free induction decay showed minimum evidence of broad components. The chemical shift was determined relative to the ^{31}P signal of phosphocreatine or to the proton resonance of water (Ackerman et al, 1981). Intracellular pH was derived from the chemical shift of inorganic phosphate (Gadian et al, 1979; Taylor et al, 1983).

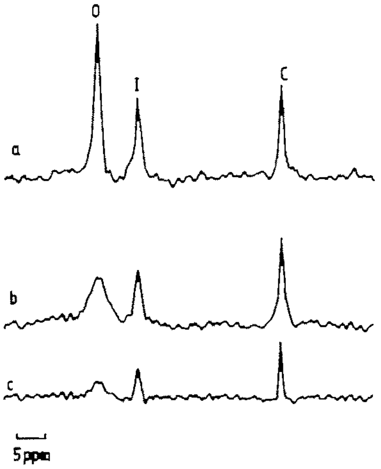

FIG. 2.

Effect of magnetic field profiling on ^{31}P spectra of a sphere consisting of three layers. The diameter of the homogeneous volume of the magnet was 10 cm in (a) and 4 cm in (b) (c) Spectrum (b) after data deconvolution C is signal from central, I from intermediate, O from outer sphere. Data were acquired with an 8 cm surface coil using a 90° pulse at coil centre. The phantom was in the centre and the coil was 5 cm below the centre of the magnet.

T_1 *measurements*

T_1 values of phosphorylated metabolites in brain were measured by saturation recovery using the sequence 90°_x, 90°_y–τ–90°–acquire. The whole-head Dadok-type coil was used and the diameter of the homogeneous volume of the magnet was set to 10 cm. Nine delay times (τ) ranging from 0.1 s to 10 s were used (total experimental time 1 h). T_1 was calculated by using a two-parameter fit to a single exponential expression:

$$A_\tau = A_\infty[1 - \exp(-\tau/T_1)]$$

where A is a signal intensity.

The two-parameter fit was appropriate because the signal levels were null at the shortest delay time. T_1 data reduction was accomplished by a least-square fitting routine.

Phantoms

The validity of the field profiling method was established by studying spectra obtained from experiments on phantoms. These consisted of three concentric glass spheres (10 cm, 8 cm and 6 cm in diameter) filled with different solutions, as discussed under Results.

RESULTS

Studies on phantoms

The three concentric compartments of the phantom were filled with 100 mM sodium pyrophosphate (inner sphere), 100 mM sodium phosphate at pH 5 (middle sphere) and 100 mM sodium phosphate at pH 9 (outer sphere). Sharp resonances were obtained from all three

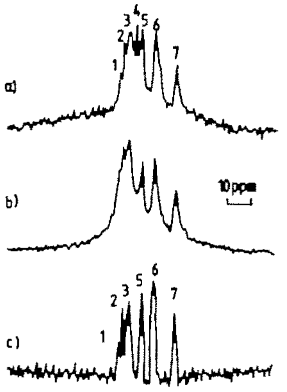

FIG. 3.

Effect of magnetic field profiling on ^{31}P spectra of liver. The diameter of the homogeneous volume of the magnet was 10 cm in (a) and 4 cm in (b). (c) Spectrum (b) after data deconvolution. Data were collected with an 8 cm surface coil using a 180° pulse at coil centre and interpulse delay of 0.5 s The coil was 5 cm away from the magnet centre. One hundred transients were accumulated for Spectrum (a) and 1024 for (b) Exponential broadening of 10 Hz was used. Peak assignments: 1 = phosphomonoesters (phosphocholine, phosphoethanolamine, sugar phosphates); 2 = inorganic phosphate; 3 = phosphodiester (presumably glycerophosphocholine, glycerophosphoethanolamine); 4 = phosphocreatine; 5, 6, 7 = γ, α, β phosphate of purine and pyrimidine triphosphates (mainly adenosine triphosphate); 6 also contains pyrophosphate of nicotinamide dinucleotides

compartments of the phantom when the diameter of the homogeneous volume of the magnet was set to 10 cm (Fig. 2a). Reduction of profiled diameter to 4 cm resulted in considerable broadening of the resonances from the outer and intermediate spheres (Fig. 2b). The broad components were removed from the spectrum by deconvolution with function $P(t)$ (see above) (Fig. 2c). T_2^* was set to 20 ms, corresponding to the measured increase in line width by 15 Hz of the resonance of the outer sphere (20 ms ≅ 1/15π Hz). Factor n was empirically determined.

Studies in humans

Figure 3 shows the effect of magnetic field profiling on ^{31}P spectra of human liver. In order to minimise respiratory movements the subject was asked to lie on the coil, which was placed in the mid-axillary line between the upper and lower margins of the liver. The distance between coil and liver as measured by ultrasound was 2 cm. When the diameter of the homogeneous volume of the magnet was set to 10 cm, a liver spectrum with a large contamination due to skeletal muscle was obtained, as evidenced by the presence of phosphocreatine (Fig. 3a). This muscle contamination could be removed by reducing the diameter of the homogeneous volume of the magnetic field to 5 cm (Fig. 3b). The spectrum obtained after magnetic field profiling consisted of sharp resonances sitting on top of a broad hump which was only in part due to the broadening effect of the static magnetic field gradients, since this hump was also observed at a homogeneous volume of 10 cm (Fig. 3a). Presumably there was also a contribution of phosphorus in bone and phospholipids which gave rise to resonances of about 50 ppm width at half height (Seelig, 1978; Gonzalez-Mendez et al, 1984; Thoma et al, 1985). The broad components were removed from the spectrum by deconvolution with function $P(t)$ in which parameters were determined empirically ($T_2^* = 1.5$ ms, $n = 3$). Phosphorus-31 spectra of liver with acceptable signal-to-noise ratio could be obtained within 8 min (Fig. 3c). A detailed peak assignment of ^{31}P liver spectra is given elsewhere (Oberhaensli et al, 1986a). Data collection at different interpulse delays (0.1 s, 0.25 s, 0 5 s, 1.0 s, 2.0 s, 4.0 s, 10.0 s) showed that the T_1 relaxation rate of phosphorus was fastest in γ- and β-ATP and slowest in phosphodiesters, and intermediate in inorganic phosphate and phosphomonoesters. At an interpulse delay of 10 s, all resonances were fully relaxed. Data acquisition at a rapid pulse repetition rate (interpulse delay 0.1 s) resulted in a preferential saturation of the phosphodiester resonance, thereby enhancing the resolution of the inorganic phosphate peak. The resonance composed of the α phosphate of ATP and the pyrophosphate of nicotinamide adenine dinucleotide (NAD) showed a markedly slower relaxation rate than the γ and β phosphate resonances of ATP, indicating a slow T_1 relaxation rate of NAD.

The reproducibility of topical MRS of liver was checked in 11 healthy subjects (Table I). For comparison, the spectra were quantified by calculating ratios of peak areas. The inorganic phosphate/β-ATP, phosphodiester/β-ATP and phosphomonoester/β-ATP ratios could be determined with a coefficient of variation of 15%, 10% and 14%, respectively. Similar coefficients of variation were obtained when one subject was investigated repeatedly on six separate days. Intracellular pH was 7.24±0.07 (mean±SD). Two subjects were examined twice using an interpulse delay of 10 s to determine the metabolite ratios free of saturation effects (Table I).

Figure 4a shows a ^{31}P spectrum of adult brain. The spectrum was obtained in 8 min by placing the surface coil on the skull overlying the posterior frontal region of the brain. Phosphorus-31 spectra of adult brain show characteristically a large phosphomonoester and phosphodiester peak whose identity has not yet been established. T_1 measurements were performed in two subjects twice. T_1 values for the inorganic phosphate, phosphomonoesters, phosphodiester, phosphocreatine and γ phosphate of ATP, were 2.5 s (2.5, 2.5), 2.8 s (2.2, 3.5), 2.4 s (2.6, 2.2), 4.8 s (4.5, 5.0) and 1.0 s (1 0, 1.0), respectively (The figures in parentheses are the results of individual measurements, the averages being given in front of the parentheses.)

The reproducibility of topical MRS of brain was assessed in eight subjects (Table I). In the posterior frontal region the phosphocreatine/β-ATP, phosphodiester/β-ATP, phosphomonoester/β-ATP and inorganic phosphate/β-ATP ratios could be measured with a coefficient of variation of 10%, 17%, 20% and 28%, respectively. Intracellular pH was 7.03 ± 0.04 (mean $\pm$SD). Similar coefficients of variation were obtained in repeated measurements in the same subject. In two subjects the metabolite ratios were determined free of saturation effects in two consecutive experiments using the whole-head coil (Table I).

The phosphocreatine/β-ATP ratio changed when the coil was moved from posterior frontal (centre of coil 5 cm above orbito-meatal line, 5 cm anterior to external meatus) to anterior frontal (5 cm above acanthus). In all the six subjects investigated under identical conditions (180° pulse at coil centre and 2 s interpulse delay) the phosphocreatine/β-ATP ratio was higher in the temporal (1.08 ± 0.03, mean$\pm$SEM) than the frontal (0.79 ± 0.08) region. Apart from possible biological reasons, this finding may have been due to saturation effects since the cortex was closer to the coil anteriorly than posteriorly. In one subject, in whom anatomical details were measured by MR imaging, the distance between coil centre and cortical surface was 0.8 cm frontally and 1.4 cm temporally.

When localisation of a particular region of the brain was not of prime importance ^{31}P spectra of brain were collected with a Dadok-type whole-head coil and the diameter of the homogeneous volume of the magnet set to 10 cm. The subject was positioned such that the homogeneous volume of the magnet was centred symmetrically around the midline and touching the vertex. Phosphorus-31 spectra of brain with acceptable signal-to-noise ratio could be obtained within 5 min.

Figure 4c shows a ^{31}P spectrum of human heart. The data acquisition time was 8 min. The coil was positioned over the thoracic wall in the region of the apex. An ultrasound scan prior to the MRS study showed the anterior left ventricular wall to be at a depth of about 3 cm. Data acquisition was not gated to the heart cycle or respiration. The spectrum shows a

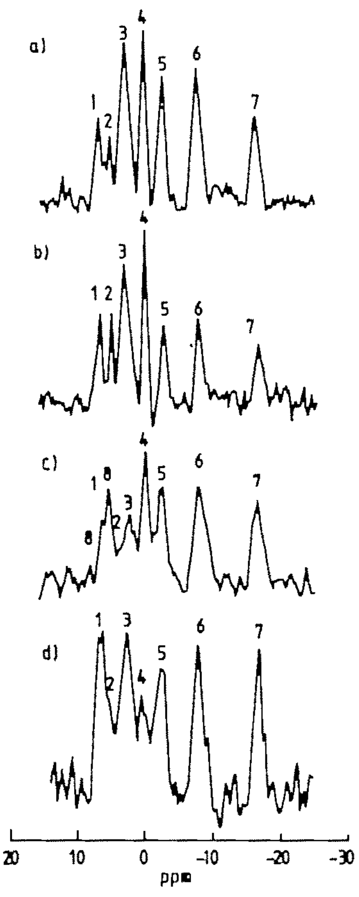

FIG. 4.

Phosphorus-31 spectrum of (a) posterior frontal brain (2 s interpulse delay, 256 transients); (b) brain (10 s interpulse delay, 32 transients); (c) heart (2 s interpulse delay, 512 transients); (d) transplanted kidney (1 s interpulse delay, 1024 transients). Spectra (a), (c) and (d) were obtained with the surface coil as in Fig. 3b. Spectrum (b) was obtained with the Dadok-type whole-head coil. Peak assignments as in Fig 3; 8 = 2,3-diphosphoglycerate.

TABLE I

RATIOS OF METABOLITE CONCENTRATIONS IN LIVER AND BRAIN AS DETERMINED BY ^{31}P MRS (MEAN $\pm$SEM)

	Liver			Brain	
Coil type	Surface coil			Surface coil*	Whole-head coil†
Interpulse delay	0.1 s	1.0 s	10 s (fully relaxed)	2.0 s	Fully relaxed
No of subjects	10	11	2	8	2
Phosphomonoester/ATP	0.33 ± 0.03	0.43 ± 0.02	0.6, 0.6	0.70 ± 0.05	0.7, 0.8
Inorganic phosphate/ATP	0.66 ± 0.04	0.72 ± 0.03	0.8, 1.0	0.36 ± 0.04	0.3, 0.3
Phosphodiester/ATP	1.1 ± 0.1	1.8 ± 0.1	3.0, 3.9	2.1 ± 0.1	1.4, 1.5
Phosphocreatine/ATP	—	—	—	1.03 ± 0.04	1.7, 1.9

* The coil was positioned 5 cm above the orbito-meatal line and 5 cm anterior to the external meatus (posterior frontal brain).

† Data were obtained with the Dadok-type whole-head coil and calculated from the saturation recovery experiment by using the values for $A(\infty)$ (cf. Methods).

phosphocreatine/β-ATP ratio of 1.5, which is close to the ratio obtained in rat heart under similar pulsing conditions (Grove et al, 1980) and which excludes a large contamination of the spectrum by skeletal muscle which would show a phosphocreatine/ATP ratio of ~3.5 (Taylor et al, 1983). However, the spectrum contains a contribution from blood as evidenced by the 2,3-diphosphoglycerate resonance which comes exclusively from erythrocytes. The peaks of 2,3-diphosphoglycerate overlap with the resonance of inorganic phosphate and make the assessment of the intracellular pH impossible.

Figure 4d shows the ^{31}P spectrum of a human kidney, which had been transplanted 6 weeks before the MRS study and was in normal functional state. The coil was placed over the right iliac fossa after the margins of the kidney had been determined by palpation. The kidney was estimated to be about 3 cm below the surface Data were accumulated for 16 min. The spectrum shows a low content of phosphocreatine which is typical of kidney and excludes a large contamination of the spectrum by skeletal muscle and intestine. The transplanted kidney seemed to contain phosphomonoesters in high concentration which is consistent with findings of studies performed *in vitro* on human cadaver kidney before transplantation (Chan et al, 1981). The low signal-to-noise ratio of the spectrum was attributed to the poor filling factor of the coil with renal tissue since the circular coil failed to match the shape of the kidney.

Discussion

This study demonstrates the use of topical MRS for obtaining localised ^{31}P spectra of various organs in humans. Topical MRS proved to be a reproducible method for obtaining ^{31}P spectra of brain and liver, requiring only a few minutes of set-up time. Phosphorus-31 spectra with acceptable signal-to-noise ratio could be obtained from about 30 ml of tissue within 10 min. Metabolite ratios characterising the energy status of liver and brain could be determined with a coefficient of variation of 10% to 20%. Only the assessment of the inorganic phosphate in brain lacked accuracy; this was due to its low intensity and its overlap with neighbouring peaks. The fact that the variations of the MRS measurements between and within individuals were similar indicates that the precision of the measurements was essentially established by the signal-to-noise ratio of the spectra. At the currently available precision of MRS measurements, only pathological lesions differing in their metabolite ratios from the norm by 20–40% are likely to be detected in a single patient. Apart from technical developments, an increase in sensitivity of MRS is expected to result from the design of specific function tests. This was demonstrated recently in experiments in which the response of the liver to a fructose load was investigated by MRS (Oberhaensli et al, 1986a).

Topical MRS could be implemented in a standard superconducting magnet, the only requirement being an extra set of gradient coils. Magnetic field profiling in combination with data deconvolution made it possible to remove most of the signals from a superficial layer of tissue of about 2 cm thickness The exclusion of the surface signal was not complete in the present study, as demonstrated in the phantom experiment shown in Fig. 2, in which signals originating at a depth of 1–2 cm were reduced by only about 70%. This was attributed to the fact that the boundaries of a homogeneous volume selected by magnetic field profiling are not spherical but, rather, star-shaped (Gordon et al, 1982). Calculation of the contours of the magnetic field showed the existence of "islands" in the periphery of the homogeneous volume of the magnet which are not affected by magnetic field profiling. To overcome these imperfections of topical MRS a 180° pulse at coil centre was generally used in studies in humans to reduce the contribution of surface signal further.

A serious disadvantage of topical MRS is that the selected volume is fixed around the geometrical centre of the magnet. Therefore, adjustments of the position of the sensitive volume can only be made by repositioning the subject. Moreover, the volume selected by topical MRS is approximately spherical and cannot be shaped to fit the anatomical structure of, for example, the left ventricular heart wall. This would be crucial to minimise the interference of erythrocyte 2,3-diphosphoglycerate with the assessment of the myocardial inorganic phosphate (cf. Fig. 3c). Methods selecting a disc-shaped volume would seem more appropriate although they, too, failed to exclude 2,3-diphosphoglycerate from the heart spectrum in the studies reported so far (Bottomley, 1985; Blackledge et al, 1987). The spherical sensitive volume of topical MRS does not seem optimal for the investigation of organs such as brain or kidney, which are formed of several histologically different layers. However, since these layers tend to be folded, it remains to be demonstrated whether methods selecting rectangular or disc-shaped volumes match the anatomical requirements better.

In topical MRS the spectra have to be deconvoluted to remove the broad resonances of the nuclei which experience the static field gradient, and this may be considered a drawback of the method. Since, however, ^{31}P spectra of brain and liver contain broad components resulting from immobile ^{31}P (Gonzalez-Mendez et al, 1984; Chang et al, 1985; Thoma et al, 1985), which on its own needs spectral deconvolution to ease data interpretation, the additional broadening induced by topical MRS only aggravates an already existing problem. Presumably more significant is the fact that the parameters of the deconvolution routines can only be derived empirically, and this introduces a subjective element into the data analysis. Clearly, deconvolution with function $P(t)$ will be inaccurate for any spectral lines which are of comparable width to the magnetic field profiling-induced broadness that is being eliminated. This is particularly the case for compounds with short T_2, such as phosphodiesters. However, peak areas of narrow spectral lines show tolerance to parameter variations, which makes the procedure relatively insensitive to operator prejudice. Spin-echo techniques which exploit the short T_2 of phosphorus in bone and phospholipids may offer a more elegant approach to elimination of these broad resonances from the spectrum (Brindle et al, 1985).

In comparison with other localisation techniques, topical MRS offers several advantages. In contrast to some methods using switched magnetic field gradients, topical MRS does not need a pre-acquisition delay to allow for stabilisation of the magnetic field. This pre-acquisition delay may introduce phase problems and signal intensity distortions due to decay of transverse magnetisation. Fourier-series depth selection uses 90° pulses ($90° + n180°$, n : integer) for data acquisition thereby excluding experiments with optimal signal-to-noise ratio. In topical MRS the choice of pulse angle is free. It is, however, important to control the pulse angle in order to standardise the effect of saturation on signal intensity.

The requirement of strong gradients makes spectroscopy of nuclei with large spectral width such as ^{13}C not directly amenable to localisation methods using switched magnetic field gradients because gradient strength is limited for safety reasons to 1 gauss/cm for experiments in humans (National Radiological Protection Board, 1983). More complex procedures, such as polarisation transfer, have to be adopted to circumvent the problem (Aue et al, 1985). In contrast, the strong static magnetic field gradients used in topical MRS should cope with the spectral width of ^{13}C as has been demonstrated in animal experiments (Canioni et al, 1983).

Topical MRS is a straightforward method and is particularly suitable for studies of large organs with uniform histological structure, such as the liver, and of diseases which uniformly affect this tissue. It is also useful for the investigation of generalised brain disorders, as has been demonstrated recently (Hayes et al, 1985). It can be used for the examination of large superficial lesions such as strokes and tumours. Alternative methods such as Fourier-series depth selection and depth-resolved spectroscopy give a different form of spatial resolution (both give disc-shaped regions at defined distances from a surface coil). It must, however, be remembered that none of the various techniques can overcome the problem of low sensitivity and can, therefore, only be used to collect signals in a time acceptable in routine patient studies from volumes of 20–30 ml. This volume needs to be larger when it is a long way from the detector coil. Signals originating from smaller regions very close to the surface can be detected by the use of small surface coils.

It is likely that, depending on the clinical problem to be examined, different forms of spatial selection will be appropriate, while, in some conditions, improvements in temporal resolution will be important. Although not generally available, static field profiling will have a role to play, particularly when nuclei such as ^{13}C, with a large spectral width, are examined.

ACKNOWLEDGMENTS

This work was supported by the Medical Research Council, the Department of Health and Social Security and the British Heart Foundation. R D O was a recipient of a grant by the Swiss National Science Foundation. D.H J was supported by Action Research for the Crippled Child. The MRS studies on transplanted kidneys were performed in collaboration with Dr P. Ratcliffe and M. Blackledge. Magnetic resonance imaging was kindly performed by Dr G. M. Bydder, Hammersmith Hospital, London.

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Book reviews

Cranial Computed Tomography in Infants and Children. By E. N. Faerber, pp. 237, 1986 (Spastics International Medical Publications, London), £16.00
ISBN 0-632-01296-X (UK)
0-397-48000-8 (USA)

Recent years have seen a plethora of new books on cranial CT (CCT). Many of these attempt to embrace all aspects of cranial CT. Frequently, paediatric CCT is dealt with at a superficial level, the specific problems relating to the paediatric patient receiving no special emphasis. This excellent book corrects this deficiency by filling this gap in the literature. Despite its size, it covers all aspects of CT and clearly reflects the author's authoritative understanding of his specialty.

Basic principles, artefacts, techniques and normal anatomy are clearly discussed in the opening two chapters. This is followed by a useful chapter on the neonate, including the development of the brain and the pre-term infant. These chapters are probably the best didactic texts on these subjects, which most radiologists have difficulty in understanding. There follow chapters on hydrocephalus, trauma, vascular disorders, CNS infection and immune deficiency disorders, tumours and metabolic and degenerative disorders. Pathological descriptions of the conditions are included as appropriate and the chapters are well illustrated, the figures being of good quality images from modern-generation machines.

This is a textbook, not another addition to the many atlases on CCT. In addition to the excellent text and illustrative material, each chapter has an extensive list of up-to-date references which, considering the size of the book (and its cost!), enhances its value further.

This is an excellent book, for both day-to-day and reference purposes, and can be recommended to all radiologists who are involved in paediatric CCT.

W St C. Forbes

Nuclear Gastroenterology Ed. by P. J. A. Robinson, pp. 180, 1986 (Churchill Livingstone, Edinburgh), £35.00.
ISBN 0-443-03255-6

This book, written by 10 specialists, presents an account of the techniques available to clinicians in the field of nuclear gastroenterology. It consists of 11 chapters: 1 scintigraphy of the oesophagus, 2 gastric emptying, 3 bile dynamics, 4 scintigraphy in diffuse liver disease, 5 scintigraphic diagnosis of liver tumours, 6 acute cholecystitis, 7 radiolabelled white cells in inflammatory disease, 8 scintigraphy in gastrointestinal bleeding, 9 radiolabelled antibodies for imaging of gastrointestinal tumours, 10 assessment of the small intestine and 11 gastrointestinal scintigraphy in paediatrics.

As the editor states in the preface, the book puts emphasis on "newer radionuclide procedures for alimentary tract investigations ..., to illustrate normal and abnormal results in terms of both physiology and anatomy, to indicate clinical applications and to emphasise the role of the new techniques in relation to existing methods of investigations." In a way these objectives are achieved. However, as expected in a book written by 10 authors, the quality and clarity of the chapters vary, and in some of them it is not immediately clear whether a proposed technique is of routine clinical value or whether its use is only for research.

The book is well printed, the images (all in black and white) are of good quality and a high standard is maintained throughout. There is also a reasonable review of the relevant medical literature. At £35.00 the book is probably overpriced, but I am sure it reflects modern prices more than the editors desire.

In summary, this is a book which gives an up-to-date review of nuclear medicine techniques in gastroenterology and should be useful to all workers in the field of nuclear medicine.

H. J Testa

The development of a system for transillumination computed tomography

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ABSTRACT

A transillumination computed tomography system has been developed for studies of the breast, testes, neonatal skull and peripheral limbs. Initial experiments on test objects have emphasised the problems of scattering and geometrical dependence of lesion detection that are likely to be encountered in conventional diaphanography, but have demonstrated the feasibility of computed tomography as a means of improving the sensitivity of the transillumination technique. The problems of transillumination computed tomography have been addressed and further areas of research identified.

The use of transillumination (diaphanography) to investigate the pathology of human organs has enjoyed a revival in recent years. It was on the early work of Cutler (1929), who emphasised the potential of transillumination primarily in the diagnosis of breast lesions but also in inflammatory diseases of the sinuses and differentiation between solid tumours and hydrocoele of the testis, that many subsequent investigators have based their work (Ohlsson et al, 1980; Carlsen, 1982; Watmough, 1982, 1983; McIntosh, 1983; Bartrum & Crow, 1984; Marshall et al, 1984; Merritt et al, 1984; Drexler et al, 1985; Geslien et al, 1985). The technique of transillumination has been further extended to include investigation of the infant skull (Martin et al, 1977; Donn et al, 1979; Johns, 1979, Arridge et al, 1985) and organs in the abdomen (Martin et al, 1977).

The method of transillumination has, until now, relied upon an intense light source transilluminating the organ of interest with the image of the shadow being formed using either direct viewing, film or low light level video camera. The image formed represents the absorption of light by different tissues of the body and research has been conducted to understand the mechanisms involved in the interaction of light with different tissues and their wavelength dependence (Cartwright, 1930; Hardy & Muschenheim, 1936; Derksen & Monahan, 1952; Clark et al, 1953; Hardy et al, 1956; Watmough, 1982; Key, 1985). It has been suggested that the increased vascularity in, for instance, breast tumour, and the relatively high absorption owing to the presence of oxyhaemoglobin is a prime determinate in the detection of tumour (Watmough, 1982).

Many imaging techniques exist for the investigation of breast lesions (Isard, 1984; Khayat et al, 1985) but it is generally accepted that only X-ray mammography has a sensitivity and specificity sufficient for use as a screening method. The work of Bartrum and Crow (1984) demonstrated that the sensitivity and specificity of detecting lesions in the breast using transillumination approached that of mammography only when used in conjunction with mammography and that detection was poor when transillumination was used by itself. Further results from these workers highlighted that transillumination conducted independently of mammography had nearly equal sensitivity for tumours greater than 20 mm but that equal sensitivity with mammography only could be achieved with transillumination for tumours less than 10 mm in size if, again, used in conjunction with mammography. These results infer that diagnostic information may be available with transillumination, but that careful extraction of data and interpretation of results is necessary if the sensitivity is to be improved.

This paper describes the development of a transillumination computed tomography system which may have a greater detection efficiency and perhaps a less operator-dependent technique. The system has been designed for preliminary studies of the breast, testes, neonatal skull and peripheral limbs.

METHOD AND MATERIALS

The system developed is illustrated schematically in Fig. 1. The light source consists of a tungsten halogen lamp (150 W) capable of delivering an output luminance of 2.8×10^7 cd m^{-2} (type LS11, Barr & Stroud Ltd). The light was transmitted via glass fibre-optic bundles (~ 5 mm diameter) to a series of optical lenses generating a beam approximately 30 mm in diameter, with an aperture restricting the effective area to approximately 3 mm in diameter. The light beam and opposing collimator were arranged to be coaxial in both translational and rotational motions. The collimator consisted of three apertures 3 mm in diameter in an encased housing, so reducing the effect of stray light and allowing the collimated light to be transmitted by another fibreoptic to a photomultiplier tube (EMI 9658R). The translational and rotational

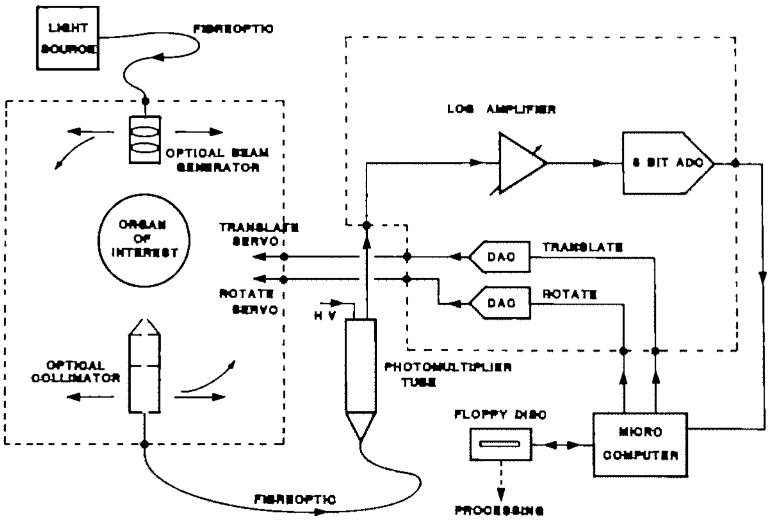


FIG. 1.

A schematic diagram of the transillumination computed tomography system

motions were controlled by a microcomputer and servo motors which were capable of generating up to 256 translational steps with rotational sampling over a maximum translational distance of 13 mm and full 360° rotation. In the work described, the system was set for 128 1 mm translational sampling and 127 rotational sampling steps over nearly 180°.

The photomultiplier tube (PMT) was sensitive to red light up to approximately 900 nm, with peak quantum efficiency at 380 nm (Fig. 2). The dynode chain for the photomultiplier tube was designed for non-pulsed operation and for coping with high light levels. The original design of the equipment envisaged high gain operation of the PMT, with sensing of the output signal to control an aperture to reduce the light levels from the source when not scanning through tissue, thus avoiding damage to the PMT. The electromechanical control of this aperture proved difficult and was changed in favour of operating the PMT over a large dynamic range of light levels, with subsequent logarithmic amplification of low light levels to accommodate the large dynamic range of signal before conversion by an 8-bit ADC with 10 μs conversion time for storage in the microcomputer. The profile data were stored on floppy disk and subsequently transferred to another system for reconstruction by standard filtered back projection using a Shepp-Logan filter without correction for attenuation. In an attempt to evaluate the potential of transillumination computed tomography, test objects were constructed from paraffin wax. Paraffin wax was selected because it could easily be formed into a variety of shapes and was thought to simulate the reflective, absorptive and scattering effects of tissue. The test objects were either planar (Fig. 3A), to assess the relative importance of the position of lesions on the profile data before reconstruction, or truncated cones simulating female breast with embedded opaque lesions (Fig. 3B) to evaluate the data acquisition and reconstruction process.

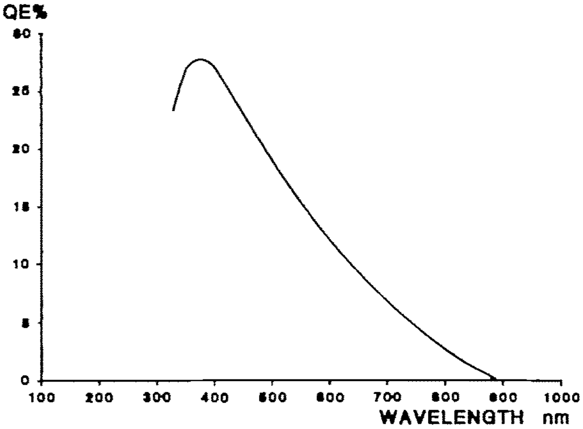


FIG 2

The spectral response of the photomultiplier tube defined by the quantum efficiency (QE) for different wavelengths.

The planar-object experiments consisted of scanning the plate of paraffin wax (5 mm thick) containing bands of opaque tape of various widths (0.5 mm, 0.8 mm, 1.3 mm, 2.5 mm and 5.0 mm), of negligible thickness, and of approximately equal separation (~ 16 mm) at different positions in 25 mm of scattering material. Subsequent to these initial experiments and in order to simulate the conditions in the three-dimensional test object, a 12 mm-wide attenuator was scanned through 5 mm, 25 mm and 45 mm of scattering media. The planar test objects were also used to obtain a measure of the attenuation characteristics of paraffin wax.

The conical test object consisted of one or two

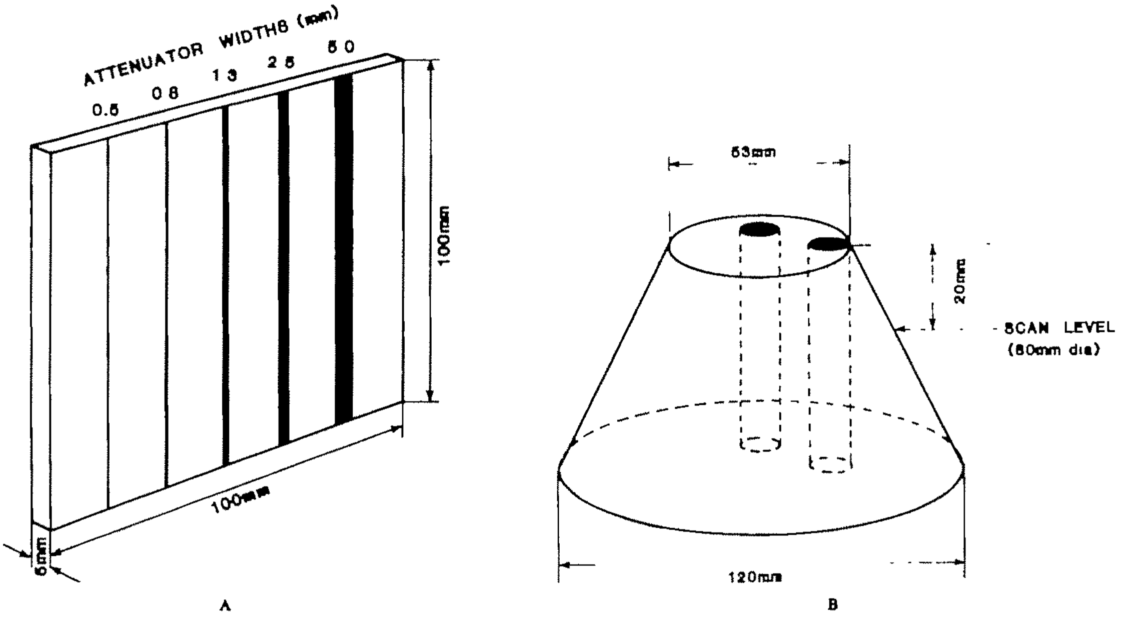


FIG. 3.

(A) The planar test object formed from paraffin wax and containing five light attenuators consisting of opaque bands of tape affixed to the surface. (B) A test object suitable for evaluating the tomographic system at different scan levels and relative position of lesions (12 mm diameter) with respect to the surface.

opaque rods, diameter 12 mm, of plastic embedded in the length of the paraffin wax. The truncated cone enabled the light path length to be varied in proportion to the diameter of the wax phantom at the scan level chosen. Depending upon the scan level, variation in the position of the "lesion" with respect to the surface was obtained.

RESULTS

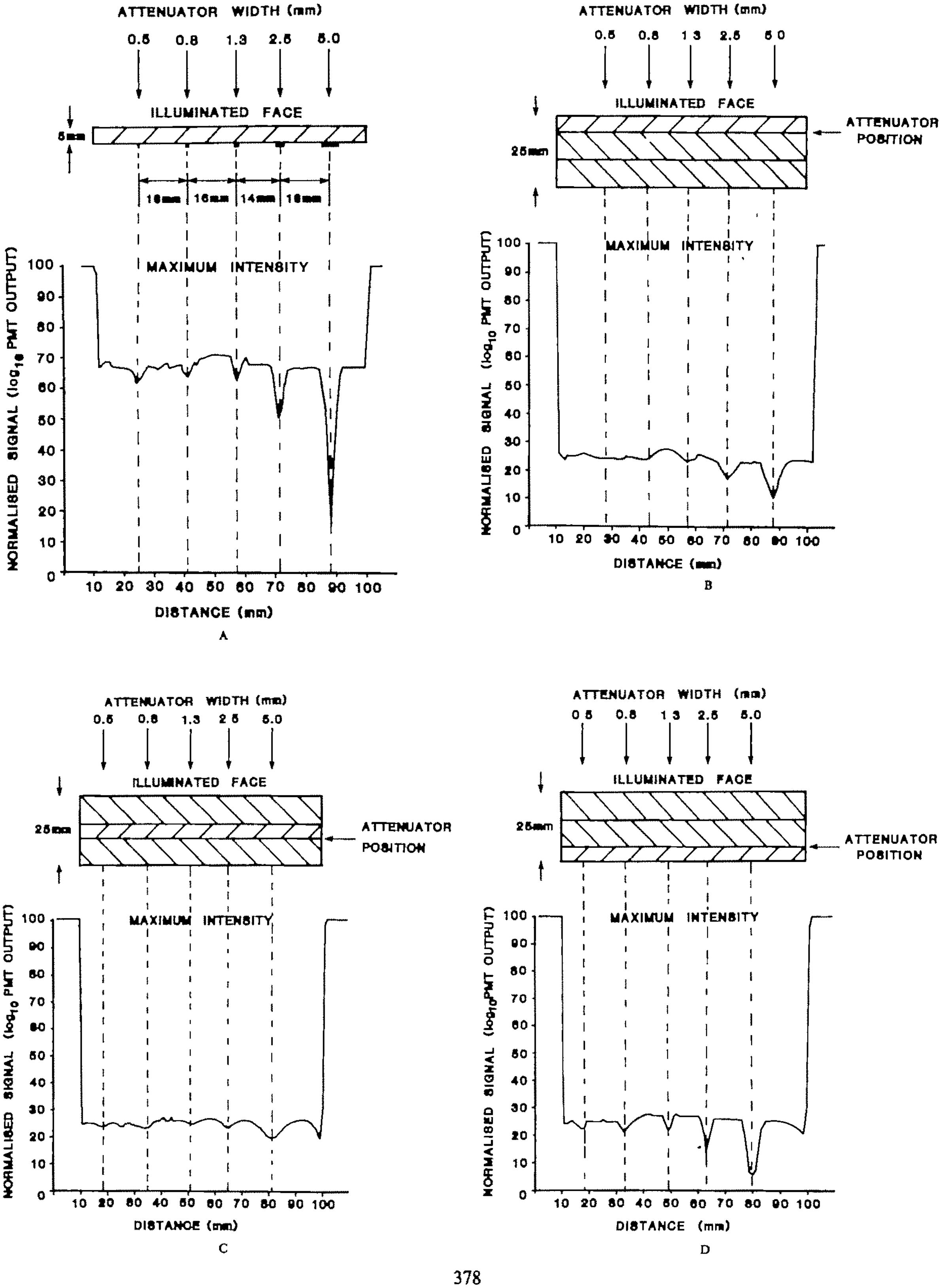
The results for the planar test objects and dependence upon the relative position of scattering media are demonstrated (Fig. 4A–D). From the scanning of the thinnest test object (Fig. 4A) it is apparent that the beam width (10 mm) on the object plane, which was 60 mm from the collimator and midway between collimator and beam generator, contributed with scattering in the paraffin wax to degrade the intrinsic resolution of the system. Although "lesion" widths of 2.5 mm and perhaps less are apparent, the relative amplitudes and shape of profiles indicate that objects of equal opacity but different size would not be faithfully reproduced in the reconstruction. The results from the 12 mm attenuator (Fig. 4E) indicate that this is probably the minimum size of lesion that could be reproduced with the system as it is presently configured.

Comparison of the relative position of the attenuators in a thickness of 25 mm of scattering indicates, from the profile data (Fig. 4B–C), that the best resolution is obtained if the attenuator is near the surface of the medium (as opposed to the central position) and that "sharper" profile data are obtained when the attenuators are positioned close to the side opposite the illuminated face. Resolution of a 5 mm attenuator is possible provided it is within 12 mm of the surface of the object. The situation is likely to be improved in clinical practice, since the three-dimensional nature of lesions, not emulated in these experiments, will aid detection. The data from the attenuator 12 mm wide (Fig. 4E) demonstrate that as the size of the lesion increases, so the thickness of the scattering medium can be increased. The extinction of light in paraffin wax, and probably tissue, is not a simple attenuation process, as demonstrated by the multiexponential curve (Fig. 4F), and is likely to represent multiple scattering processes.

A result from the reconstruction of an object containing two "lesions" of 12 mm diameter and scanning through approximately 80 mm of paraffin wax (Fig. 5) demonstrated that an attenuator about 15 mm from the surface was relatively well resolved compared with the attenuator 20 mm from the surface. No attenuation correction protocol has been incorporated within the reconstruction algorithm. The appearance of a band of apparently high attenuation around the image of the edge of the test object is typical.

CONCLUSIONS

The preliminary results presented demonstrate that the principle of transillumination computed tomography can be realised in practice and that it may be


ATTENUATOR WIDTH (mm)
0.5
0.8
1.3
2.5
5.0
ILLUMINATED FACE
5mm
16mm
16mm
14mm
16mm
25mm
ATTENUATOR POSITION
MAXIMUM INTENSITY
NORMALISED SIGNAL ($\log_{10}$ PMT OUTPUT)
0
10
20
30
40
50
60
70
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DISTANCE (mm)
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A

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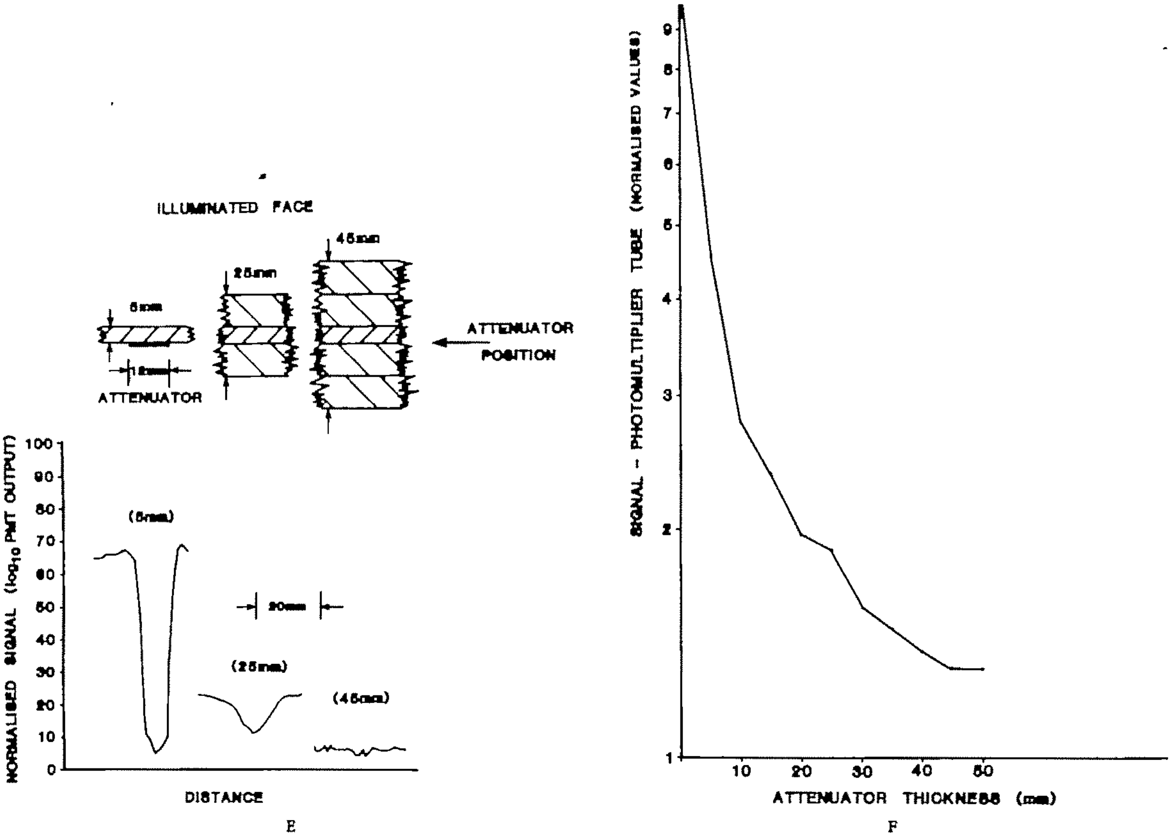

FIG. 4

Profile data from (A) a 5 mm-section test object, (B) the same test object as in (A) but with further scattering material (20 mm) after illumination; (C) the same test object as in (A) with further scattering material both before (10 mm) and after (10 mm) illumination; (D) the same test object as in (A) but with bulk of scattering material before illumination (20 mm); (E) a 12 mm-wide attenuator with varying degrees of scattering thickness. (F) The relationship between the output signal from the photomultiplier tube and the thickness of the attenuator.

useful if applied to clinical situations. From this work it is apparent that multiple scattering and the relationship to lesion position influences the sensitivity of conventional transillumination techniques, but that correction for both attenuation and the effects of relative position of lesions may be possible with computed-tomography techniques and so yield a greater sensitivity overall.

Before this technique can be applied clinically, however, redesign of the equipment may be necessary to improve both resolution and signal strength. The planar-object experiments demonstrated that the spatial resolution of the present equipment is limited by the beam width in the object plane and the degree of collimation achieved at reception. Therefore it may be expedient to select a collimated laser diode of the correct wavelength to achieve both a fine beam comparable to half the diameter of the object to be detected, while also improving the peak light output through tissue and consequent detected signal. The choice of a single wavelength or combination of discrete wavelengths to accentuate the differential effects and wavelength dependency of light interaction with tissue will be an important consideration in the design of future equipment. With pulsed lasers it may also be possible to derive transit-time images representing the scattered radiation path length and hence give some indication of the underlying pathology. Moreover, it may be feasible in this system to obtain blood-flow maps throughout the volume of an organ by means of the Doppler effect in either reflection or transmission.

Another problem to be addressed is the "edge effect" in the reconstructed image. The apparent attenuation near the surface of the object is probably due to reflection at the air/paraffin-wax interface. The design of the test objects has resulted in a smooth, "shiny" surface which is unlikely to be so great in the clinical situation. Any consideration given to coupling the system optically to the object may give benefits in

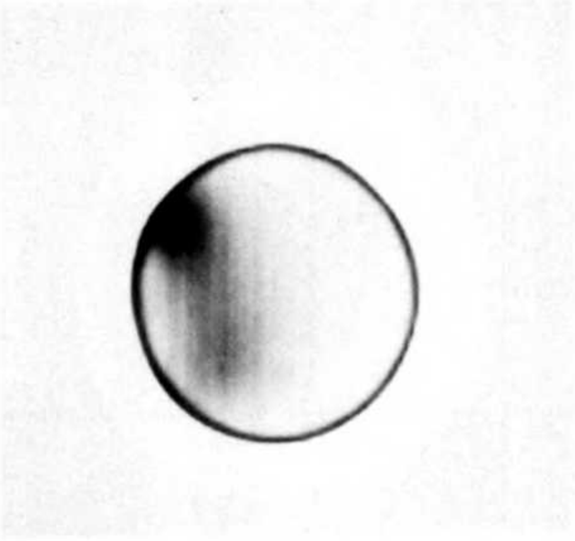

Fig. 5.

A transaxial reconstruction of a paraffin-wax test object containing two lesions of 12 mm diameter, situated approximately 15 mm (top left) and 20 mm (bottom left) from the surface.

reducing surface artefacts and improving signal strength, but may have the disadvantages of causing geometrical distortion and an increase in the complexity of scanning.

In summary, it is apparent that the methods of transillumination have yet to be fully understood and exploited. The technique of computed tomography has the potential to resolve many of the physical problems of transillumination and, thus, to improve the sensitivity of the technique.

Acknowledgments

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A comparison of clonogenic and radionuclide uptake assays for determining the radiation response of human small-cell lung cancer xenografts and cell lines

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ABSTRACT

Previous work has suggested that a radionuclide (^{3}HTdR) uptake assay can provide a measure of drug and radiation sensitivity comparable with that given by the clonogenic assay. We have now extended this work to examine the radiation response of human small-cell lung cancer xenografts and cell lines with a wide range of plating efficiencies Preliminary experiments using cultured cells indicated that irradiation of a single-cell suspension following disaggregation generally produced similar response data to those obtained when cultures were irradiated *in situ* and subsequently disaggregated The response of eight cell lines to a single dose of 2 Gy was measured using both radionuclide uptake and clonogenic assays. There was no correlation between the two sets of data Agreement between the radiation–response curves obtained using ^{3}HTdR uptake and clonogenic assays was better for high plating efficiency xenografts (NCI-H69, COR-L51) than for low plating efficiency xenografts (COR-L24, COR-L31). Radionuclide uptake indicated very shallow response curves for the low plating efficiency lines. Altering the time of radionuclide addition from the standard Day 4 to other times between Day 2 and Day 6 did not greatly change the indications of radioresponsiveness provided by the assay Growth-curve experiments for line COR-L24 showed that cell numbers at Day 4 after irradiation with 1.5 Gy or 3 Gy were very similar to those in unirradiated cultures. For NCI-H69, however, the cell numbers were very different for the different radiation doses It appears that a high proportion of cells in lines such as COR-L24 take many days to show radiation damage as measured by reduced ^{3}HTdR uptake.

Clonogenic cell survival and radionuclide uptake assays have both been advocated as methods of predicting clinical tumour response to radiation or cytotoxic drugs (Hamburger et al, 1978; Friedman & Glaubiger, 1982; Sondak et al, 1984). Clonogenic assays (Hamburger & Salmon, 1977; Courtenay & Mills, 1978) have a number of marked operational disadvantages. Many tumour specimens are difficult to disaggregate into single-cell suspensions and frequently have very low plating efficiencies. In addition, a period of several weeks must be allowed for colony growth before a result is obtained. The tritiated thymidine (^{3}HTdR) uptake assay of Friedman and Glaubiger (1982) overcomes these disadvantages to some extent in that an absolute single-cell suspension is not required and the result is obtained in 5–6 days. The proportion of tumour cells which contribute towards the end-point in this assay is also much larger than that in the clonogenic assay Several groups have shown that radionuclide uptake assays can provide a measurement of drug and radiation sensitivity comparable with that obtained using clonogenic assays (Tanigawa et al, 1982; Friedman et al, 1983; Sondak et al, 1984).

We have recently described studies carried out in our laboratory in which we have measured the radiation and drug response of well characterised experimental tumour systems using both clonogenic and radionuclide uptake assays (Twentyman et al, 1984). The two assays produced good agreement over one and a half to two decades of response for both an established mouse tumour and a high plating efficiency human tumour xenograft Similar results have been reported from studies using a human ovarian xenograft of low plating efficiency (Hanson et al, 1985). Our work has now been extended to examine the radiation response of human small-cell lung cancer lines with a wide range of plating efficiencies.

MATERIALS AND METHODS

Cell cultures

A range of established human lung cancer cell lines derived in this laboratory were used in the study (Baillie-Johnson et al, 1985) Small-cell lines COR-L24, COR-L31, COR-L32, COR-L47 and COR-L51 conventionally grow as floating aggregates in RPMI 1640 medium supplemented with 10% fetal calf serum, penicillin and streptomycin (Gibco Biocult Ltd). Small-cell line COR-L88 grows loosely attached to tissue-culture plastic and large-cell line COR-L23 grows as a tightly attached monolayer on plastic, both in the same medium as above.

For the purposes of comparison, NCI-H69, a small-cell lung cancer line (kindly supplied by Dr D. Carney) and MOR, a lung adenocarcinoma line (kindly supplied by Dr M. Ellison), were used. The former grows as floating aggregates while the latter forms a monolayer on plastic, both growing in the same medium as above. Two established mouse tumour cell lines, EMT6/Ca/VJAC and RIF-1, were also used. Both of these lines grow attached to plastic in Eagles MEM supplemented with 20% new-born calf serum (Gibco Biocult Ltd).

Single-cell suspensions were prepared by treatment for 15 min at 37°C with 0.4% trypsin and 0.02% versene in phosphate-buffered saline. Following the addition of excess medium containing serum, the cells were spun down at 200g for 5 min, the supernatant discarded and the pellet resuspended in medium. Dispersion of the cells was achieved by pipetting or by drawing the suspension through a 10 ml syringe fitted with a 25 gauge needle. If any clumps remained, the suspension was passed one or more times through a glass funnel packed with sterile cotton gauze until a single-cell suspension was achieved. Counts of phase-contrast viable cells were carried out using a haemocytometer. Xenograft tumours of small-cell lines were grown in MF1/Nu nude mice (OLAC 1976 Ltd). Tumours were initiated by the inoculation of 2–5 × 10^6 cells from culture into the gastrocnemius muscle of the hind leg in a volume of 0.05 ml of Hanks balanced salt solution. Tumours grown from cell lines derived in this laboratory reached a size of 500 mm^3 in a period of time which varied from 4 months to 11 months. Tumours from an inoculation of NCI-H69 cells reached a size of 500 mm^3 at 2–4 weeks after injection.

Each tumour was excised under sterile conditions and minced with scissors. A single-cell suspension was prepared by agitating the material in medium with 1 mg/ml of neutral protease (Sigma Type IX) for a period of 1–2 h (Twentyman & Yuhas, 1980) and filtering through cotton gauze.

Radiation treatment

The cell lines were maintained in culture by weekly passage. Experimental flasks were set up 2–3 days before treatment so that they were in exponential growth phase at the time of treatment. Immediately before irradiation, a single-cell suspension was prepared in growth medium and 6 ml of the suspension was placed in a 25 cm^2 tissue-culture flask on the surface of a bucket of crushed ice. The flask was exposed to incremental doses of X rays. After each dose, 0.5 ml of the suspension was taken into a plastic tube and kept on ice. The cells were assayed at the end of the treatment.

In order to compare the radiation response of line COR-L47 before and after disaggregation, five flasks containing growing aggregates of cells were prepared 3 days before treatment. Four of the flasks were irradiated before single-cell suspensions were prepared, while aggregates from the remaining flask were reduced to a single-cell suspension and then irradiated in this condition. When the line COR-L88 was used in a similar experiment, five flasks were prepared 3 days before treatment. Four flasks were irradiated with the cells growing as exponential monolayers. A single-cell suspension was prepared from the remaining flask and subsequently irradiated with incremental doses of X rays. All irradiation treatments were carried out using 250 kV X rays at a dose rate of 0.6 Gy/min.

^{3}HTdR uptake assay

The basic method was that described by Friedman and Glaubiger (1982) as modified by Twentyman et al (1984) and using RPMI 1640 medium with 10% fetal calf serum. In brief, 35 mm Petri dishes (Falcon Plastics) were prepared with a bottom layer of 1 ml medium containing 0.5% agar (Difco Agar Noble). The cells were then added in a further 1 ml of liquid medium. The number of cells plated in each dish depended on the doubling time of the cells and varied from 2 × 10^3 for EMT6/Ca/VJAC to 2 × 10^5 for slower-growing small-cell lines. These numbers were chosen on the basis of preliminary experiments to determine, for each cell line, the relationship between ^{3}HTdR uptake and number of cells plated. The number used was always on the linear portion of such a curve (Twentyman et al, 1984). The plates were incubated at 37°C in a humidified atmosphere of 8% CO_2 and 92% air. Four days later 20 μl of ^{3}HTdR stock solution (1.85 MBq/ml, 1.81 TBq/mmol) (Amersham International) was pipetted into each of the dishes, which were then returned to the incubator for a further 24 h. At the end of this time the cell suspension was removed from each dish using a Pasteur pipette, the agar surface was rinsed with phosphate-buffered saline and the washings and suspensions were centrifuged at 500g for 10 min. The samples were then prepared for liquid scintillation counting on a Nuclear Chicago Isocap 30 counter, according to the method described by Twentyman et al (1984).

The radiation response of NCI-H69 and COR-L24 after irradiation at 3, 10, 30 and 100 Gy was measured using ^{3}HTdR uptake during different periods of 24 h during the subsequent 7 days. In these experiments 20 μl of stock ^{3}HTdR was added to various groups of dishes either immediately after irradiation or at 24, 48, 72, 96, 120 or 144 h later. The cells were returned to the incubator for 24 h after the addition of the ^{3}HTdR and then assayed as above.

Clonogenic assay

The clonogenic assay was essentially that of Courtenay and Mills (1978) in which low oxygen tension and the addition of rat red cells were used to optimise clonogenicity, with modifications as described by Twentyman et al (1984). Different numbers of cells (from 200 to 10^4) were plated for different cell lines according to their plating efficiency. The incubation time also varied between the cell lines, ranging from 3 weeks to 6 weeks.

Growth curves after irradiation

Growth-curve experiments using irradiated NCI-H69 and COR-L24 cells were set up in order that changes in actual cell numbers could be related to the results of the ^{3}HTdR uptake assay for radiation response Single-cell suspensions of NCI-H69 and COR-L24 were irradiated with 1.5 Gy or 3 Gy of X rays and one control group was not irradiated. Dishes were then prepared containing

10^5 cells/dish in the case of NCI-H69 and 5×10^5 cells/dish in the case of COR-L24 from each suspension. Cell numbers were then counted in duplicate dishes after 2, 4, 6, 8, 10 and 12 days.

RESULTS

Time of disaggregation

Results of experiments to compare the response of line COR-L47 and COR-L88 irradiated either as growing cultures or following disaggregation into single-cell suspensions are shown in Fig. 1. The plating efficiencies of both of these lines are in the region of 40% and they are therefore regarded as high plating efficiency lines.

The radiation response of COR-L47 measured by the clonogenic assay showed close agreement between cells disaggregated before and after irradiation. Response measured by the ^{3}HTdR uptake assay did not show quite as close an agreement. Values of cell survival or fractional ^{3}HTdR uptake lay between 0.17 and 0.32 after 3 Gy in the case of COR-L47 and between 0.18 and 0.34 in the case of COR-L88.

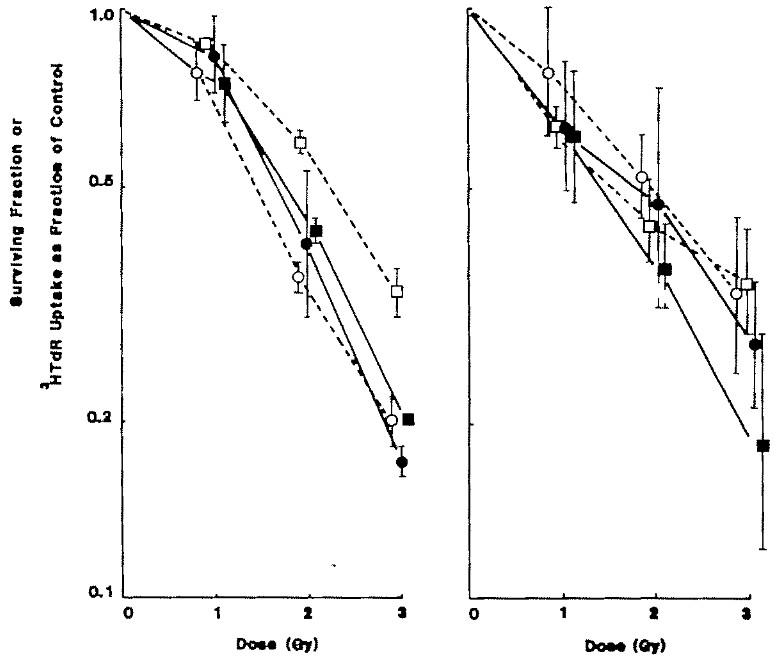
Radiation response of small-cell and non-small-cell lines

Table I shows the results from experiments which measured the response to 2 Gy of mouse tumour, human small-cell lung cancer lines and human non-small-cell lines. Data from experiments where response values, for both the Courtenay cloning assay and the ^{3}HTdR assay, were obtained from the same cell suspension are shown in Fig. 2. The correlation coefficient between the results of the two assays based

TABLE I

SURVIVING FRACTION OF EIGHT LINES AT 2 GY

Cell line	Experiment No.	^{3}HTdR uptake	Clonogenic survival
EMT6/Ca/VJAC	1	–	0.71
	2	0.88	–
	3	0.89	0.65
RIF-1	1	–	0.57
	2	0.11	–
	3	0.64	0.70
MOR	1	–	0.54
	2	0.77	0.45
	3	0.81	0.32
COR-L23	1	–	0.36
	2	0.49	0.46
	3	0.44	0.71
COR-L32	1	0.69	0.14
	2	0.70	0.28
	3	0.81	0.33
COR-L47	1	0.43	0.48
	2	0.50	0.33
	3	0.46	0.35
COR-L88	1	0.49	0.35
	2	0.34	0.34
	3	0.56	0.40
COR-L51	1	0.53	0.18
	2	0.43	0.26
	3	0.42	0.26



A B

FIG. 1.

Radiation response of small-cell lines (A) COR-L47 and (B) COR-L88 measured by either clonogenic assay (closed symbols and solid line) or ^{3}HTdR uptake assay (open symbols and broken lines). Circles indicate irradiation of cells growing as intact aggregates or monolayers; squares indicate irradiation of single-cell suspensions following disaggregation (see Materials and Methods). Points are mean values of two experiments (A) with error bars showing individual values or three experiments (B) with error bars showing ±2 standard errors

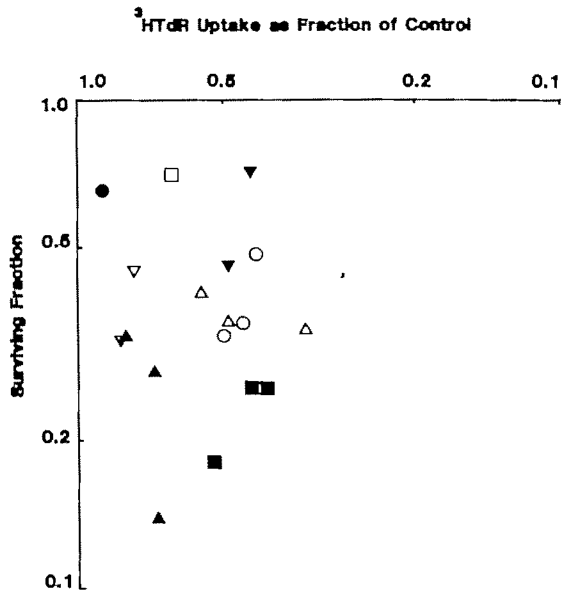


FIG 2.

Response of eight cell lines to 2 Gy as determined by clonogenic and ^{3}HTdR uptake assays. ● EMT6/Ca/VJAC, □ RIF-1, ▽ MOR, ▼ COR-L23, ▲ COR-L32, ○ COR-L47, △ COR-L88, ■ COR-L51 Correlation coefficient = −0.09.

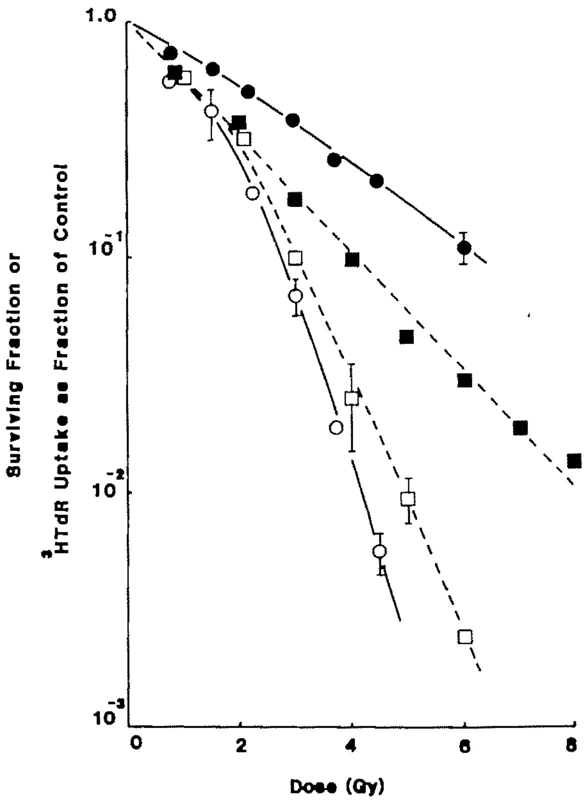


FIG. 3.

Radiation response of high plating efficiency xenografts NCI-H69 (■, □) or COR-L51 (●, ○) as measured either by the clonogenic assay (□, ○) or ^{3}HTdR uptake assay (■, ●). Data are from single experiments. Points for ^{3}HTdR uptake show mean values for three dishes and error bars are ±2 standard errors. In most cases the error bars are smaller than the dimensions of the symbols. Points for clonogenic cell survival are based on counts of three tubes and error bars show two standard errors based on the Poisson distribution of the total colony count.

on these data was −0.09, indicating essentially no correlation.

Radiation response of cells from xenograft tumours

The radiation responses of cells from xenograft tumours with relatively high and low plating efficiencies are shown in Figs 3 and 4. The clonogenic survival curves all showed around a 2 log cell-kill at a dose of 6 Gy. The curves obtained using the ^{3}HTdR uptake assay, however, differed quite considerably from one another. After a dose of 5 Gy, ^{3}HTdR uptake as a fraction of control for NCI-H69 was 5% compared with a value of 35% for COR-L24. The relatively high plating efficiency (PE) xenografts NCI-H69 (PE ~60%) and COR-L51 (PE ~ 20%) gave a closer agreement between the clonogenic assay and ^{3}HTdR uptake assay results than did the relatively low plating efficiency xenografts COR-L31 (PE ~ 2.5%) and COR-L24 (PE ~ 3.2%). We obtained similar results when the radiation response of the cell lines NCI-H69 and COR-L24 growing *in vitro* was measured (results not shown).

^{3}HTdR uptake during a 7-day period

The response to 3, 10, 30 or 100 Gy of NCI-H69 and COR-L24 cells growing *in vitro* was determined using the ^{3}HTdR uptake assay but varying the time of ^{3}HTdR addition. The radionuclide uptake by unirradiated cells is shown in Table II and the effects of irradiation are shown in Fig. 5A (NCI-H69) and B (COR-L24). In the case of NCI-H69 there was a decrease in ^{3}HTdR uptake for all radiation doses; after 30 Gy and 100 Gy the limit of detection for ^{3}HTdR uptake was reached by Day 2 and after 10 Gy by Day 4. After 3 Gy, ^{3}HTdR uptake was 20% of that of the control cells by Day 2, 10% by Day 4 and had increased to 20% by Day 6.

In the case of COR-L24 there was a rapid decrease in ^{3}HTdR uptake after 100 Gy and this fell progressively to below the limit of the assay by Day 4. After the lower doses there was a slight decrease in uptake at Day 0. However, there was no difference at Day 1 or Day 2 between the uptake for control cells and cells irradiated with 3, 10 and 30 Gy.

After 3 Gy, ^{3}HTdR uptake was approximately 60% of that of the control cells at Day 4 and Day 6. After 10 Gy the uptake was 35% at Day 4 and 30% at Day 6

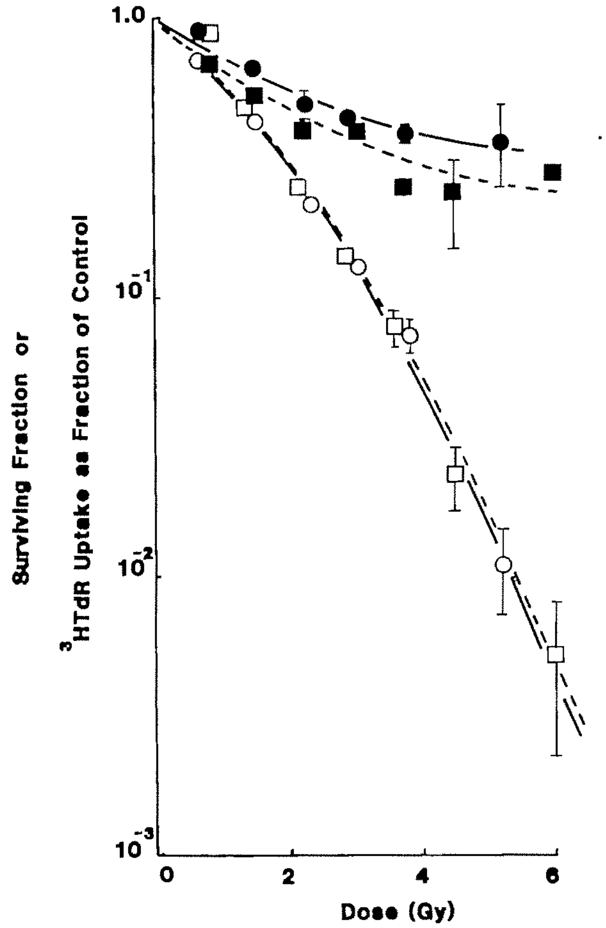


FIG 4.

Radiation response of low plating efficiency xenografts, COR-L24 (●, ○) or COR-L31 (■, □) as measured either by the clonogenic assay (□, ○) or by ^{3}HTdR uptake assay (■, ●). Points and error bars as defined in Fig. 3.

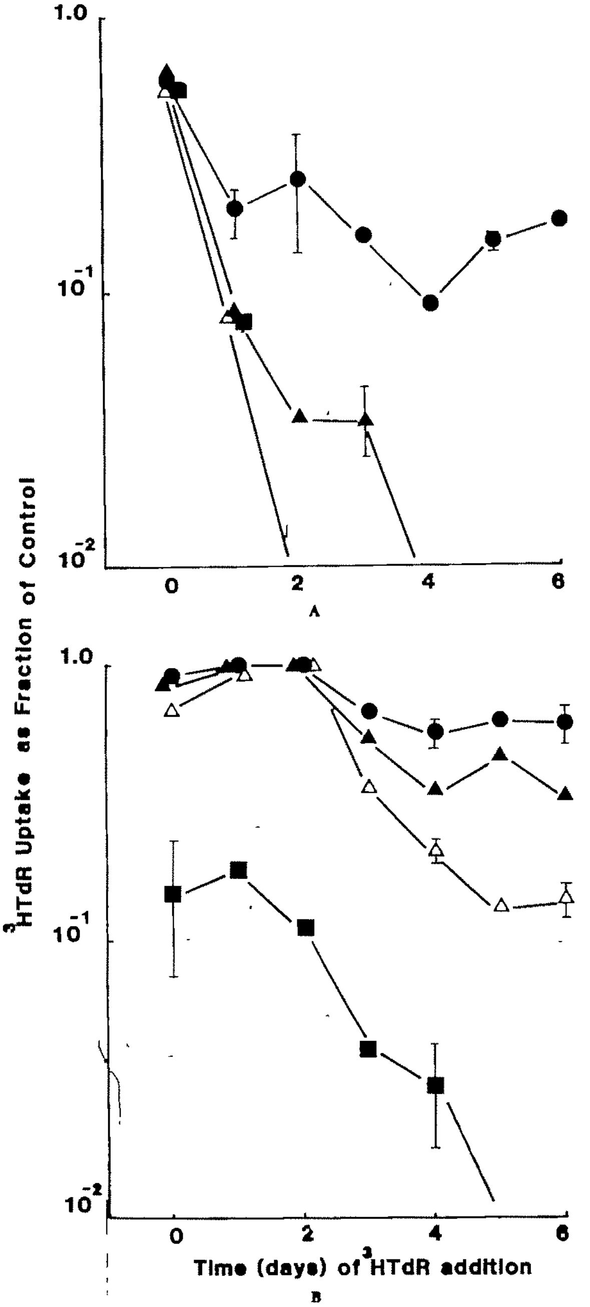


FIG 5.

Radiation response of small-cell lines (A) NCI-H69 and (B) COR-L24 determined using the ^{3}HTdR uptake assay with the radionuclide being administered at different times after irradiation with ● 3 Gy, ▲ 10 Gy, △ 30 Gy, ■ 100 Gy. Points are mean values for three dishes and sample error bars are ±2 standard errors

TABLE II

^{3}HTdR UPTAKE BY UNIRRADIATED CELLS AT VARIOUS TIMES AFTER PLATING

Day of ^{3}HTdR addition	24 h ^{3}HTdR uptake (cpm × 10^3)*	
	NCI-H69	COR-L24
0	1.51	0.54
1	4 18	0.79
2	5 68	0 93
3	10.36	1.54
4	19 96	2.12
5	21 41	2 03
6	24.84	2.00

*Mean value for three dishes.

and after 30 Gy the values were 20% and 14%, respectively.

Growth curves after radiation treatment

The growth curves of cell lines COR-L24 and NCI-H69 after irradiation with 1.5 Gy or 3 Gy and of the control are shown in Fig. 6. After plating at 10^5 cells/dish, control cells of line NCI-H69 showed an initial lag phase before reaching exponential growth and cell numbers of 4×10^6 by Day 8. After 3 Gy the lowest cell number was reached at Day 4, increasing by Day 6 and reaching 2.4×10^5 by Day 8. The cell numbers at Day 4 were very different for the control cells and irradiated cells.

Control cells of line COR-L24 showed a much longer initial lag phase after plating at 4×10^5 cells/dish. The lowest cell number was reached by Day 4, after which cell numbers increased to 2×10^6 by Day 8. After 3 Gy the lowest cell number was reached by Day 6 Cell numbers then increased to approximately 5.5×10^6 at Day 8 before slowly declining. The cell numbers at Day 4 remained very much the same for the control cells and for cells after radiation treatment.

A second experiment, using triplicate dishes for each point and extended to 16 days, gave similar results (not shown). After 3 Gy the cell numbers of COR-L24 were still slowly declining at Day 16 while the cell numbers of NCI-H69 were rapidly increasing.

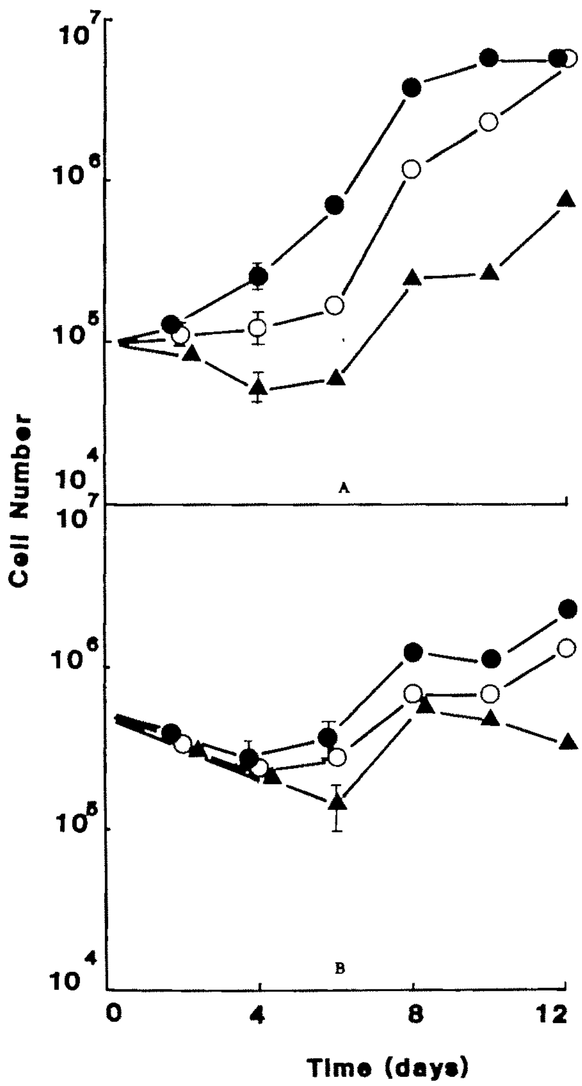


FIG 6

Growth curves of small-cell lines (A) NCI-H69 and (B) COR-L24 with time, after being set up at (A) 10^5 cells/dish or (B) 5×10^5 cells/dish ● Control, ○ irradiated with 1.5 Gy, ▲ irradiated with 3 Gy. Points shown are means of two dishes and sample error bars show the individual values

DISCUSSION

These experiments were designed to compare the use of clonogenic and ^{3}HTdR uptake assays for determining the radiation response of lung tumour xenografts and cell lines. The ^{3}HTdR uptake assay has a number of theoretical and practical advantages compared with the clonogenic assay as a predictive test for short- and medium-term clinical response. In addition to a much shorter assay time and the absence of a requirement for an absolute single-cell suspension, the ^{3}HTdR assay involves a much larger proportion of the cell population in the result of the assay. It also overcomes the "all or nothing" effect of the clonogenic assay whereby a colony of 50 cells will contribute the same as a colony of many hundreds of cells to the result of the assay.

For either assay it would be necessary to disaggregate a clinical sample before exposing the cells to radiation. Therefore we examined whether there was a difference in apparent radiation response between aggregated and disaggregated cells from lines COR-L47 and COR-L88. Our experiments indicated that the response measured from disaggregated cells would show a reasonable agreement with the response which would have been obtained from intact samples.

The work of Fertil and Malaise (1981) has indicated that sensitivity to a radiation dose of 2-Gy *in vitro* correlates with the clinical radioresponsiveness of different tumour cell types. In addition, Carney et al (1983) have observed a two- to fivefold difference in survival between small-cell and non-small-cell lung cancer lines following irradiation at 2 Gy We therefore examined whether the ^{3}HTdR uptake assay could, for a range of cell lines, produce a ranking of sensitivity to 2 Gy similar to that produced by clonogenic assay. There was, however, no correlation between data for the two assays and the proportional decrease in ^{3}HTdR uptake was generally considerably less than the reduction in clonogenic cell survival. The two assays do not appear to be interchangeable for this purpose.

Over a range of radiation doses the agreement between the assay results for high plating efficiency xenografts was closer than that for low plating efficiency xenografts. Whereas Friedman et al (1983) (using Chinese hamster cells *in vitro)* obtained similar radiation–response curves for a standard colony assay and the ^{3}HTdR uptake assay over several log orders of cell-kill, Twentyman et al (1984) found good agreement between the assays only over one and a half to two decades of response following radiation treatment of cells from NCI-H69 xenografts. Hanson et al (1985) have compared the clonogenic assay and the ^{3}HTdR assay in measuring the response of low cloning efficiency human ovarian tumour xenograft cells. They also found agreement only over the first two decades of response. Such lack of agreement may reflect the different parameters being measured by the assays but may also be partially because of the different cell populations which contribute to the response measured. Whereas the clonogenic assay only measures the response of the clonogenic cells within a population, a much larger number of cells with very limited capacity for DNA synthesis and/or proliferation may contribute to the result of the ^{3}HTdR uptake assay. If the response of the non-clonogenic cell population is different from that of the clonogenic cell population in terms of inhibition of proliferation, then we would expect to find a poorer correlation between the results of the two assays as the proportions of clonogenic cells decrease. Most clinical tumour samples are likely to have very low plating efficiencies and hence the possibility of a lack of correlation between results using the different assays is very great.

Four days has been used as a standard assay time for ^{3}HTdR uptake (Friedman & Glaubiger, 1982; Twentyman et al, 1984; Hanson et al, 1985). It has, however, been suggested that, when slow-growing cell lines or biopsy specimens are treated and ^{3}HTdR uptake is measured at 4 days (that is after maybe only one or two divisions), the cells may still be in a temporarily radiation-perturbed state, but that, if several generation times are allowed to elapse, the effect of such temporary perturbations may become less pronounced (Hanson et al, 1985). We therefore studied the effect of changing the time between irradiation and carrying out the ^{3}HTdR uptake assay. When 24 h ^{3}HTdR uptake was measured at various times after irradiation of COR-L24 (low plating efficiency) or NCI-H69 (high plating efficiency) cells, the uptake was similar between Days 4 and 6. Hanson et al (1985) also measured ^{3}HTdR uptake by cells at 4, 5 or 6 days in culture following 1 Gy or 3 Gy of radiation and found similar effects at all times. It does not, therefore, appear that changing the day of assay can greatly change the indications of radioresponsiveness provided by the ^{3}HTdR assay.

Cell population growth curves over a period of 12 days following irradiation showed that manifestation of radiation response followed very different time courses in cell lines NCI-H69 and COR-L24. At Day 4 the cell number for NCI-H69 was considerably affected by the radiation. Clear differences in numbers for COR-L24 did not, however, begin to be seen until Day 6. It seems likely that a high proportion of cells in cultures of this line take a considerable time to manifest radiation damage in terms of reduced ^{3}HTdR uptake compared with unirradiated controls.

Although previous work (Twentyman et al, 1984) has suggested that the ^{3}HTdR uptake assay can provide a measure of drug and radiation sensitivity comparable with that measured by the clonogenic assay in well defined tumour systems, we have now found that, in some cases, particularly in the case of low plating efficiency tumour xenografts and cell lines, the measurement of radiation response by the clonogenic and ^{3}HTdR uptake assays produced very divergent results. It may be that in these cases there is a considerable subpopulation of cells which contribute to the result of the ^{3}HTdR uptake assay and not to that of the clonogenic assay. These cells do not show much radiation-induced reduction in ^{3}HTdR uptake when assayed at Day 4 and may, hence, obscure the response of a smaller but more affected population of clonogenic cells. On the other hand, a cell line in which all proliferative cells show a rapid fall in ^{3}HTdR uptake following irradiation will appear to be more sensitive when the response is measured at Day 4. If tumours growing *in vivo* contain only a small proportion of clonogenic cells and a much larger proportion of cells with a limited proliferation potential, then it may well be that the ^{3}HTdR uptake assay may provide a better indicator of the early to medium-term tumour response. The ultimate fate of an irradiated tumour will, however, be determined only by the response of the clonogenic cells with unlimited proliferative potential. Use of the two assays together for clinical specimens should elucidate their respective roles in predicting tumour radiation response patterns.

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Technical note

Noise reduction in ultrasonic images by digital filtering

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Ultrasonic images exhibit a characteristic granular pattern, called speckle, which bears little resemblance to the actual acoustical tissue microstructure (Burckhardt, 1978). This phenomenon is due to the phase-sensitive addition, by the transducer, of echoes scattered by tissue inhomogeneities of size and spacing too fine to be resolved (Morrison et al, 1980). In the literature, speckle has been treated as a distracting artefact (Wells & Halliwell, 1981) which limits the detection of low-contrast lesions (Smith & Lopez, 1982). The mean grey-scale level of speckle provides information about the tissue echogenicity and is a feature one wants to preserve. However, the spatial variation of speckle (texture) characterises the imaging system as well as the tissue itself. Factors such as grey-scale mapping of the scanner, transducer focusing pattern and relative position, or even the intervening tissue have a significant effect on image texture (Jaffe & Harris, 1980; Kimme-Smith & Jones, 1984) so that it becomes very difficult to isolate the true tissue information contained in texture. As a consequence, judgements about the clinical significance of texture can be misleading. It seems, therefore, justified to regard speckle as noise and seek methods of obtaining a speckle-free image.

The majority of the techniques proposed for speckle suppression are based on the principle of obtaining multiple images of the same object under different imaging conditions, so that they have independent speckle patterns, and then averaging the images to reduce speckle contrast. These techniques include spatial compounding, where the target region is scanned either from different spatial locations of the same transducer (Sommer & Sue, 1983; Shattuck et al, 1984) or by several transducers (Kerr et al, 1986), and frequency compounding where the transmitted frequency is varied from frame to frame (Magnin et al, 1982). A speckle reduction feature which has been recently incorporated into commercial scanners is the recursive averaging of successive ultrasonic frames. This can be regarded as a form of spatial compounding since it is the transducer's displacement relative to the body which generates independent speckle patterns and provides speckle reduction. We have carried out a clinical trial of the recursive averaging technique on 75 patients to evaluate its performance. The results indicate that, although in some cases a modest improvement in image quality can be expected, in general recursive averaging is only of limited value. This is because speckle reduction is accompanied by blurring of the image and loss of resolution.

Alternatively, speckle suppression can be achieved by means of computer image processing (Dickinson, 1982; Bamber & Daft, 1986). Ultrasonic images are heavily corrupted by noise, yet possess well defined edges and sharp contrast. For such types of images, a noise-smoothing algorithm must be able to provide adequate noise reduction without degrading the overall quality of the image by blurring the edges or wiping out information. Our experience with several algorithms, from the simple local mean filter to more sophisticated digital filters which were designed to have a specified frequency response, has shown that algorithms which perform the same type of operation on all parts of an image cannot satisfy both requirements. As researchers have become aware of the inadequacy of fixed (space-invariant) algorithms, new techniques have emerged which adapt the filter's smoothing characteristics to changes in the local properties of the image. An evaluation of some of them (Mastin, 1985) confirms the importance of image sharpness to a human observer and the superiority of adaptive techniques over their space-invariant counterparts. The majority of the adaptive algorithms are based on linear filtering techniques, *i.e.* they replace a pixel by a linear combination of the neighbours. In this communication, a new adaptive non-linear algorithm based on median-type filters is described. It is called the adaptive weighted median filter and has been successfully applied to suppress speckle in ultrasonic images.

METHODS

The median filter is applied to a digitised image by replacing each pixel (x,y) by the median value of all the pixels contained in a pre-defined neighbourhood of (x,y). The neighbourhood is usually a square window of, say, 7×7 pixels, having its centre at the pixel (x,y). Although relatively recent in respect to linear techniques, the median filter has become very popular and has been extensively used for noise-smoothing purposes in many areas, including medical imaging

(Ioannidis et al, 1984; Morikubo et al, 1985) because of its ability to introduce considerably less blurring to the edges than linear filters. The weighted median filter derives from the median filter by introducing the concept of the weight coefficients $\{w_i\}$. The weighted median of a sequence of terms $\{X_i\}$ is defined as the median of the extended sequence which is formed by taking each term X_j, w_j times. For example, if $w_1 = 2$, $w_2 = 3$, $w_3 = 2$, the weighted median Y_{wm} of the sequence $\{X_1, X_2, X_3\}$ is given by

$$Y_{\mathrm{wm}} = \text{median}\ \{X_1, X_1, X_2, X_2, X_2, X_3, X_3\} \quad (1)$$

It has been shown (Loupas, 1987) that the selection of the weight coefficients represents a trade-off between noise smoothing and signal preservation. Maximum noise reduction is achieved when all the weight coefficients are equal, whereas when the weight coefficients decrease as we move away from the centre of the window, the preservation of edges and small details improves at the expense of noise suppression. This property permits the design of an adaptive weighted median algorithm which takes into account the space-varying characteristics of the image by selecting the weight coefficients according to the local statistics inside the window. For a $2K+1 \times 2K+1$ point window the weight coefficient w_{ij} at position (i,j) is given by

$$w_{ij} = c_1(1 - c_2 d/(\mathrm{SNR})^2) \quad (2)$$

where d is the distance of the point (i,j) from the centre of the window $(K+1, K+1)$

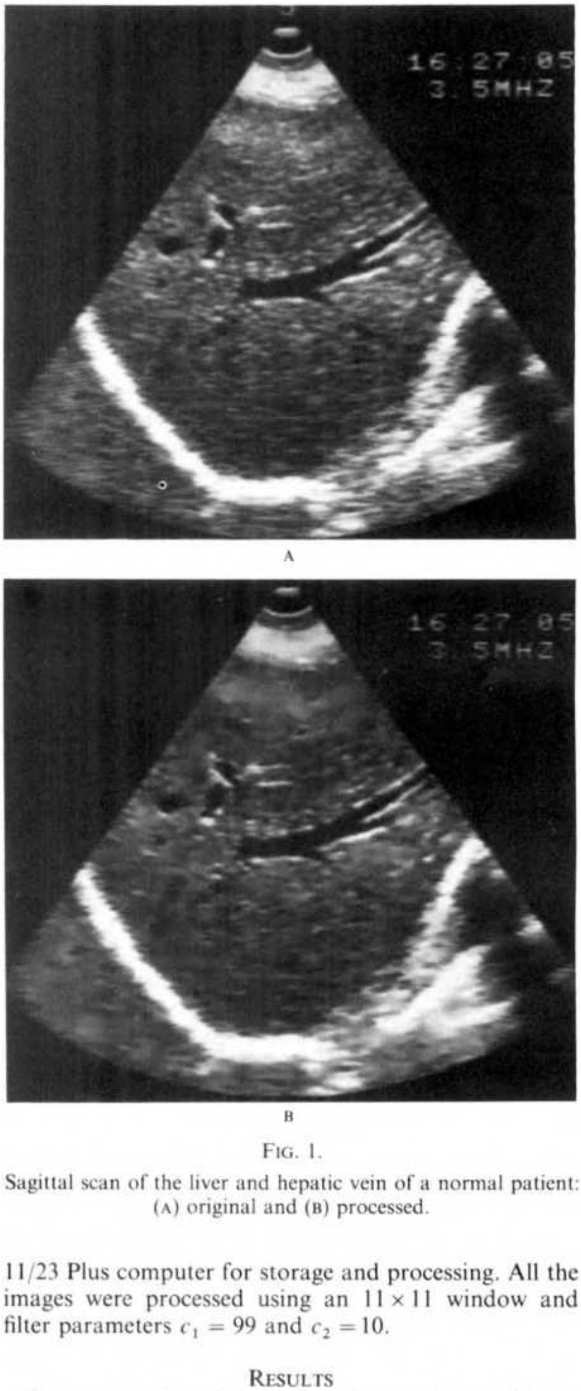
$$d = [(K+1-i)^2 + (K+1-j)^2]^{1/2} \quad (3)$$

c_1, c_2 are scaling constants, and SNR is defined as the ratio of the mean m over the standard deviation, σ, of the terms inside the window.

$$\mathrm{SNR} = m/\sigma \quad (4)$$

A low SNR value implies the presence of an abrupt discontinuity such as an edge or other resolvable structure. In this case, the weight coefficients are adjusted accordingly to provide more signal preservation instead of noise reduction. On the other hand, in uniform areas where speckle is the main source of variance in the data, the SNR is high and maximum noise smoothing is performed. Boundaries between areas of slightly different echogenicity can still be maintained, even if the SNR does not differ substantially from that of a uniform area, because of the excellent edge-preserving properties of median-type filters.

In order to assess the algorithm's performance, several abdominal ultrasonic scans have been processed. The scans were obtained by using the GL Ultrasound Ltd Z/S Series and Siemens Sonoline SX real-time sector scanners with 3.5 MHz transducers and were recorded on a video cassette recorder during the clinical examination. The scans were then digitised to $530 \times 576 \times 8$ bits resolution and transferred to a PDP 11/23 Plus computer for storage and processing. All the images were processed using an 11×11 window and filter parameters $c_1 = 99$ and $c_2 = 10$.



A

B

FIG. 1.

Sagittal scan of the liver and hepatic vein of a normal patient: (A) original and (B) processed.

RESULTS

Some examples of the processing are shown in Figs 1–3. Figure 1 is a sagittal scan of normal liver and the hepatic vein. From Fig. 1(B) it can be seen that speckle has been removed while the edges are as sharp as in the original and features like small vessels have been retained. The filter is highly capable of improving the detectability of subtle grey-scale variations within the

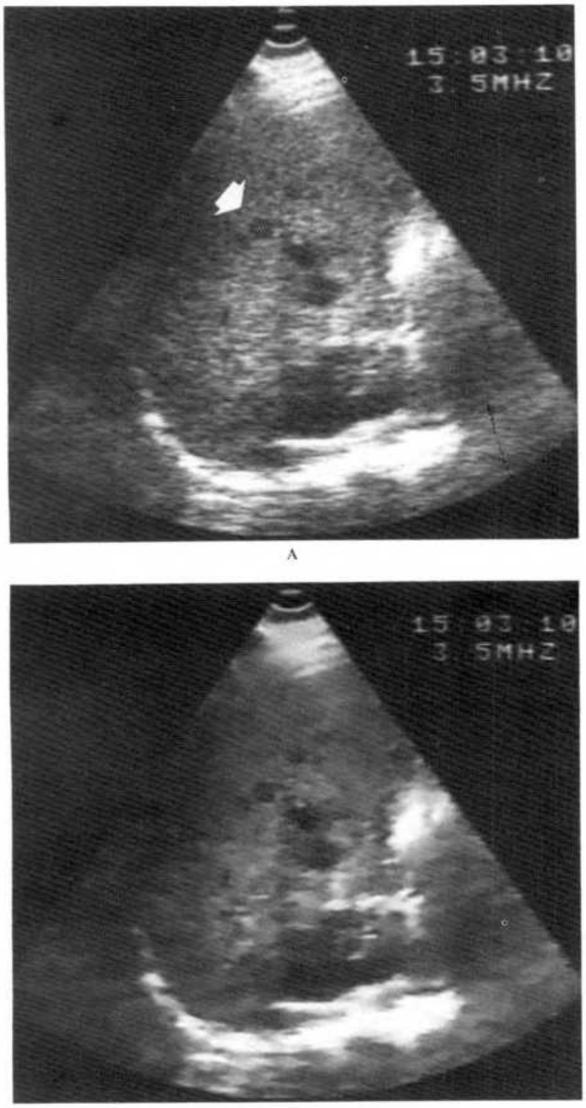


FIG. 2.

Secondary metastasis in the liver of a patient with breast cancer. The arrow indicates the presence of a tumour: (A) original and (B) processed.

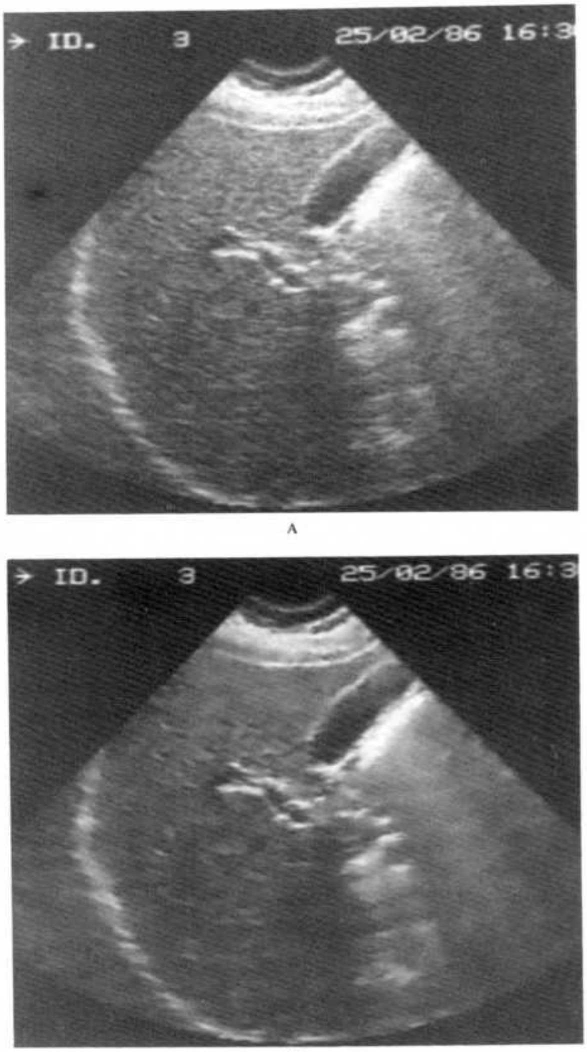


FIG. 3.

Real-time scan of the liver and gallbladder: (A) original and (B) processed.

parenchyma. Careful comparison between the processed and unprocessed image reveals that in the absence of speckle these variations become apparent. The same comment can be made about Fig. 2, which shows secondary metastasis in the liver. The area above and to the right of the tumour, indicated by the arrow, includes a hypoechoic area which is not visible in the original but stands out clearly in the processed image. Figure 3 demonstrates the effect speckle has on the resolution of small structures in the parenchyma. Portal tracts, previously obscured by speckle, can be seen better after speckle suppression.

CONCLUSION

The adaptive weighted median filter described is capable of suppressing speckle, yet, unlike space-invariant techniques, it preserves the sharpness and retains the structural information of the original image. Application of the filter to abdominal ultrasonic scans has shown that processing improves the detectability of subtle grey-scale variations within the parenchyma, increases the visibility of small structures and seems to enhance the amount of information obtained from an image. Images free from speckle noise are significantly different from those normally encountered in ultrasonic scanning. Initially, lack of familiarity results in difficulty of interpretation. However, this problem is reduced as experience of the processed images grows. Adaptive weighted median filtering has demonstrated that speckle-free images can be produced with a negligible loss of genuine image detail. The value of these processed images will be ascertained by future clinical trials.

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Case reports

Imaging and treatment of disseminated neuroblastoma with ^{131}I-meta-iodobenzylguanidine

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A 7-year-old girl presented in August 1983 with a 4-month history of diffuse limb pains, loss of weight and general malaise. The pain had commenced in the neck and progressed to involve the right shoulder, both legs and spine. Examination revealed two firm right-sided cervical lymph nodes, 1 cm in diameter, and some smaller, firm nodes palpable over the occiput and in the inguinal regions. There was diffuse abdominal tenderness in the left upper quadrant but no other abnormal findings.

Initial investigation showed a haemoglobin level of 7.9 g/dl (normochromic film), white cell count 5.9×10^9/l, ESR 90 mm in 1 h. Twenty-four-hour assay of 4-hydroxy-3-methoxymandolate was increased above 30 μmol/24 h (normal laboratory range < 30 μmol). Metadrenalin assay was 3.7 μmol/24 h (normal laboratory range up to 7 μmol). Cystathionine was not detected in the urine. Chest radiography showed an enlarged left hilum associated with extensive paravertebral widening, and abdominal radiography showed calcification in the right suprarenal region. Skeletal survey identified multiple lytic areas involving mainly the metaphyses of the long bones and skull vault. There was a calcified area anterior to the pole of the right kidney on ultrasonography and also a left paravertebral mass indenting the pelvis of the left kidney. Bone marrow aspiration confirmed marrow involvement with tumour cells occupying some 40% of the nucleated cells. Metastatic neuroblastoma was diagnosed from cervical node biopsy. The primary was presumed to be within the right adrenal gland.

The patient was treated with eight courses of OPEC over 7 months (vincristine, cisplatinum, VM26, cyclophosphamide). After an allergic response to VM26 in Course 2, VP16 was substituted without subsequent toxicity. Following chemotherapy, the right adrenal gland and an attached tumour were removed at laparotomy. Histology of this showed undifferentiated neuroblasts to be present but there were also many more differentiated cells seen. Metastatic surveillance showed no other evidence of disease and the marrow was clear both histologically and on screening with UJ13A monoclonal antibody at the ICRF Oncology Laboratory (Institute of Child Health).

Eight months after initial presentation she was treated with total body irradiation (1000 cGy) and high-dose melphalan (110 mg/m^2) and was given an autologous marrow transplantation. The marrow was treated *in vitro* with the monoclonal antibody UJ13A in an attempt to remove any residual tumour cells before reinfusion.

Subsequent progress was good with no evidence of disease until 1 year later when she developed recurrence of cervical and occipital lymphadenopathy. Despite a normal peripheral blood film, bone marrow was found to be infiltrated and fresh lytic lesions were seen on skull radiography and she rapidly developed severe head and limb pains. Imaging of the extent of the disease was carried out using ^{131}I-meta-iodobenzylguanidine (^{131}I-mIBG; 20 MBq (0.5 mCi)) and this revealed widespread tumour deposits in the skull, spine, pelvis and tibia (Figs 1, 2).

She was given 1850 MBq (50 mCi) of ^{131}I-mIBG as a therapeutic trial with rapid symptomatic relief. However, symptoms returned within 3 weeks and she was, therefore, given a further injection of 6000 MBq (150 mCi) which, again, produced rapid pain relief. Total absorbed dosage to individual organs was estimated as: skull, 6700 cGy; pelvis and spine, 5380 cGy; liver, 950 cGy. However, there is considerable uncertainty in these dosage estimations because of the inaccuracy of estimates of tumour volume. If tumour was responsible for most of the measured liver uptake (as is possible), the absorbed dose to normal liver is likely to have been below 300 cGy. Similarly, absorbed dose to marrow not infiltrated by tumour is likely to be substantially less than the calculated dose to spine, which assumes uniformity of distribution of the radioactivity in the marrow. There was no evidence of thyroid or liver dysfunction (thyroid uptake had been blocked with Lugol's iodine) but anaemia and thrombocytopenia developed, requiring repeated transfusions. She remained well for a further 3 months, during which time she was able to go away on holiday with her family.

After 3 months she once again developed severe bone pain and headache. Radiographs showed progression of the lytic changes in the skull and long bones. Pain relief

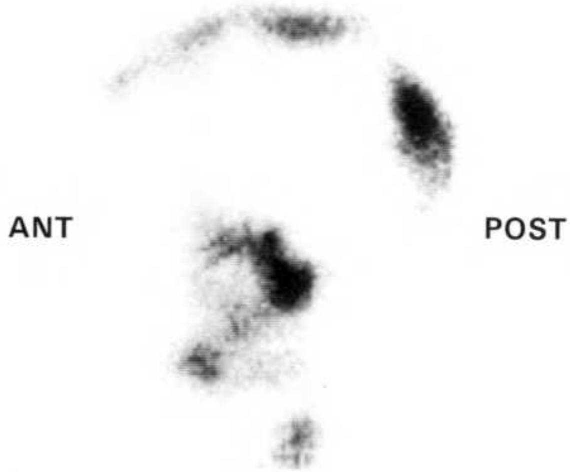

FIG. 1.

^{131}I-mIBG scan: left lateral skull 48 h post-injection showing increased uptake, particularly in the occipital region.

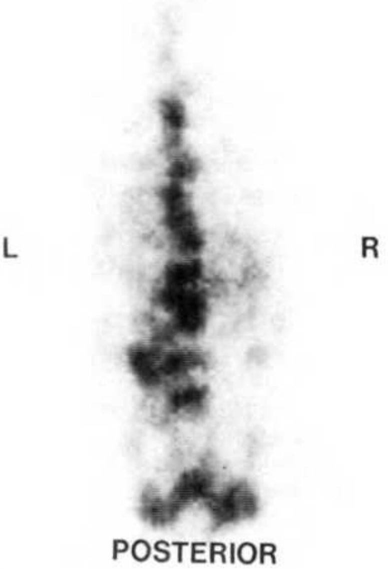

FIG. 2.

^{131}I-mIBG scan: spine and pelvis 48 h post-injection showing marked uptake in the vertebral column and pelvis.

was obtained with opiate analgesics and she died peacefully at home 1 month later.

DISCUSSION

Stage IV neuroblastoma continues to have a poor prognosis and even with modern intensive chemotherapy its 5-year survival is only of the order of 20% (Pritchard & Kemshead, 1983). New strategies, including intensive chemotherapy with or without total body irradiation, and autologous marrow transplantation, have been used in an attempt to improve these dismal results (Helson, 1985). Since most patients relapsing after chemotherapy do so at metastatic sites, sensitive methods for the detection of disease would be a useful adjunct to monitoring progress. The radiopharmaceutical ^{131}I-labelled meta-iodobenzylguanidine (mIBG) is readily taken up by $\alpha 2$ adrenergic receptors. It has been demonstrated to be of clinical use in the imaging of phaeochromocytoma and its metastases (Sisson et al, 1981; Sutton et al, 1982). It has also been used in the imaging of neuroblastoma (Hattner et al, 1984; Geatti et al, 1985). There are increasing reports of its use in the radiopharmaceutical treatment of malignant phaeochromocytoma but, as yet, few reports of its use in the treatment of disseminated neuroblastoma (Sisson et al, 1984; McEwan et al, 1985).

In this case mIBG was extremely effective in imaging the extent of the disease, as other workers have found. By combining imaging with measurements of uptake and turnover rate it also gave some indication of what radiation dose might be achievable in tumour, and also which might be the critical organ. Therapeutic dosage did produce rapid symptomatic relief. The fact that this was short-lived was almost certainly related to the extent of tumour load present at relapse. If metastatic disease could be shown to be present by such imaging and bone marrow transplantation was contemplated, then the use of a therapeutic dose of mIBG should enable larger doses of irradiation to be delivered to the tumour directly than can be achieved by standard total body irradiation. This may be particularly useful where the tumour cells are more differentiated as mIBG uptake is likely to be greatest in these cells. In this way the results of autologous bone marrow transplantation might be improved with reduction of toxicity. It does appear that the bone marrow is the critical organ. If mIBG could be used at a stage when there was less bone marrow involvement then problems with anaemia and thrombocytopenia might not arise.

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Congenital hemicerebral arterial ectasia complicating unilateral megalencephaly

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Cerebral arterial ectasia, also called megadolichoartery (Boeri & Passerini, 1964), aneurysmal malformation (Scott & Stauffer, 1964), or fusiform arterial dilatation (Eldevik & Gabrielsen, 1975), is a relatively rare condition most commonly occurring in the carotid and vertebro-basilar systems (Greitz & Lofstedt, 1954, Hulten-Gyllensten et al, 1959; Boeri & Passerini, 1964; Sacks & Lindenburg, 1969; Goldstein & Tibbs, 1981; Yu et al, 1982; Tsukamoto et al, 1985; Yamada et al, 1985).

The abnormality is characterised by pathological tortuosity, elongation, and dilatation of the arteries at the base of the brain (Hulten-Gyllensten et al, 1959; Bladin & Donnan, 1963; Boeri & Passerini, 1964; Sacks & Lindenburg, 1969; Banna & Romeo, 1979; Goldstein & Tibbs, 1981; Tsukamoto et al, 1985)

We recently encountered an interesting case with arterial ectasia showing generalised dilatation of the entire arterial tree but confined to the right cerebral hemisphere accompanying the ipsilateral hemimegalencephaly. This association is the first, to our knowledge, appearing in the neuroscience literature.

The main purpose of this report is to present an unusual finding concerning this disease.

CASE REPORT

A 23-year-old woman was admitted to Osaka Rosai Hospital in February 1985 complaining of right exophthalmos following a transient neurological episode.

Six months before admission, she had experienced sudden onset of paraesthesiae over the left side of her face, oral cavity, and left arm. These symptoms had lasted for approximately 20 min and then completely resolved. Similar episodes ensued with increasing frequency, becoming associated with right-sided headache and left hemiparesis

Results of neurological examination on admission were almost normal and she had no symptoms. Her blood pressure was normal and she had no sign of atherosclerosis.

Bilateral common carotid and vertebral angiography revealed generalised ectasia of the whole arterial tree in the right hemisphere, including anterior, middle and posterior cerebral arteries and their branches, whereas those of the other side were normal In addition, the posterior, lateral and medial choroidal arteries and perforating branches of the right side were also affected, but on neither side were the internal carotid, vertebral or basilar arteries involved There were no signs of arterio-venous malformation. Circulation times of both hemispheres were thought to be equivalent because no difference in maximum concentration time of the injected opaque substance was evident between the two sides at angiography (Figs 1–3).

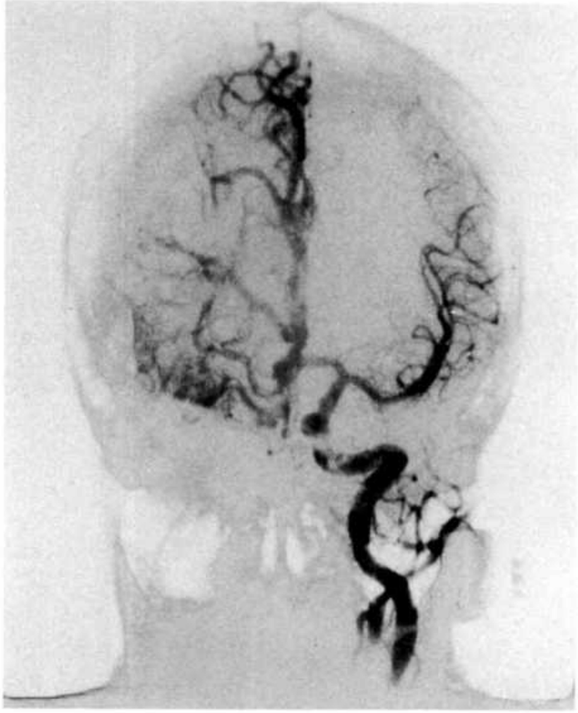


FIG. 2.

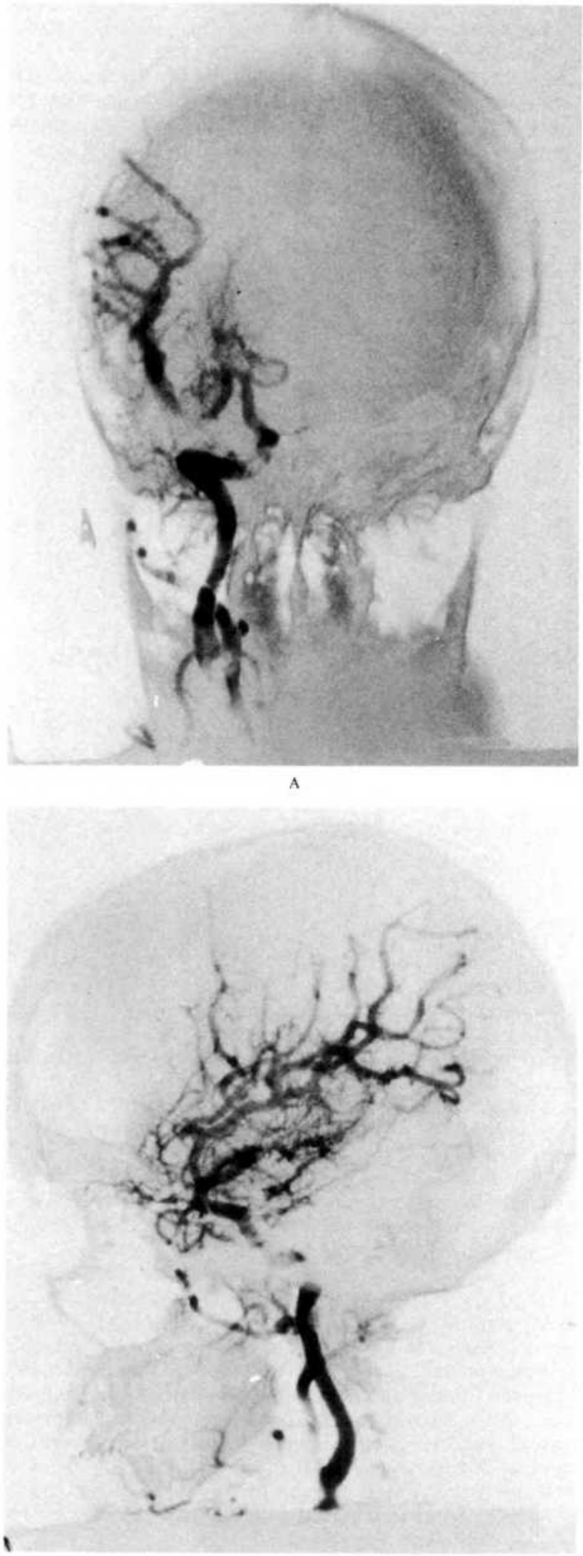
Frontal view on vertebral angiography showing generalised dilatation of the right anterior cerebral artery supplied by cross-filling via the anterior communicating artery; the arterial system of the left hemisphere was virtually normal. The left internal carotid artery was normal.

Computed tomography revealed right hemimegalencephaly, and a post-contrast infusion scan showed abnormal, diffuse spotty enhancement. There was no evidence of leukodystrophy, lysosomal disease, subdural fluid retention, hydrocephalus or any mass lesion leading to the macrocephaly (Fig. 4).

Consecutive dynamic CT images showed intense enhancement of the arteries in the right cerebral hemisphere in the arterial phase. Phase difference of time dilution curves between both hemispheres was not seen, whereas the peak height of the affected hemisphere was higher than the other (Figs 5, 6).

These findings from cerebral angiography and dynamic CT suggested that there was increased circulation volume without prolonged circulation time in the affected hemisphere, possibly accounting for the hemimegalencephaly.

The patient's symptoms have not altered since discharge and she is being followed as an outpatient.



A

B

FIG. 1.

Frontal (A) and lateral (B) views on right common carotid angiography showing generalised dilatation of the right middle cerebral arterial tree and perforating arteries in the basal ganglia. No filling of the right anterior cerebral artery was seen. The right internal carotid artery was normal in size.

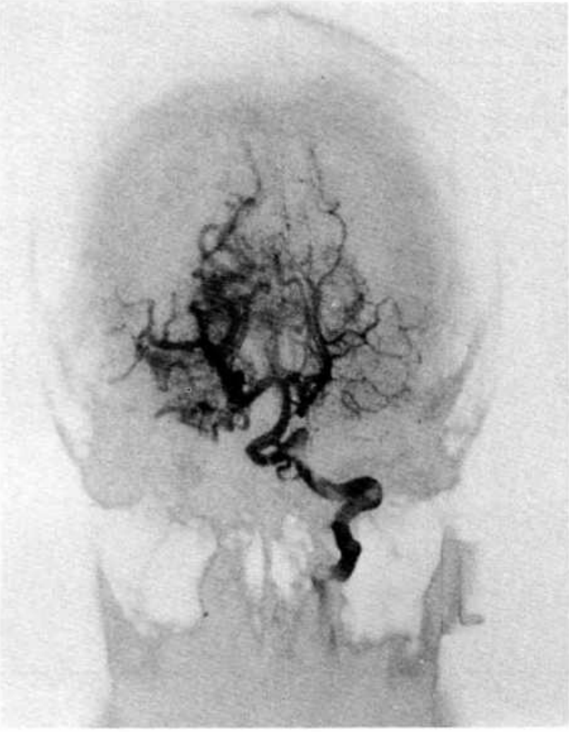


FIG. 3.

Frontal view on vertebral angiography showing marked dilatation of the right posterior cerebral artery and its branches including the right posterior medial and lateral choroidal arteries. The left posterior cerebral artery was normal in size. The verbebral and basilar arteries were also normal.

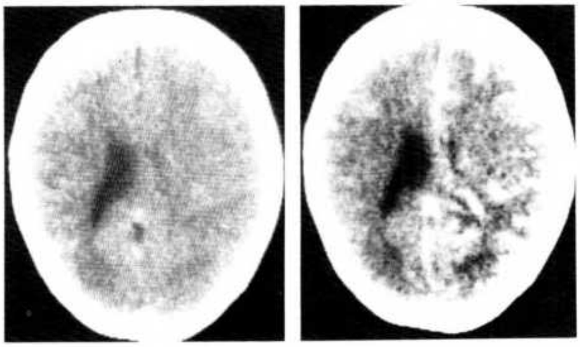


FIG. 4.

Plain (left) and enhanced (right) CT at the level of the body of the lateral ventricle. Megalencephaly was seen in the right hemisphere resulting in partial collapse of the right lateral ventricle. Enhanced CT showed abnormal diffuse enhancement in the right hemisphere.

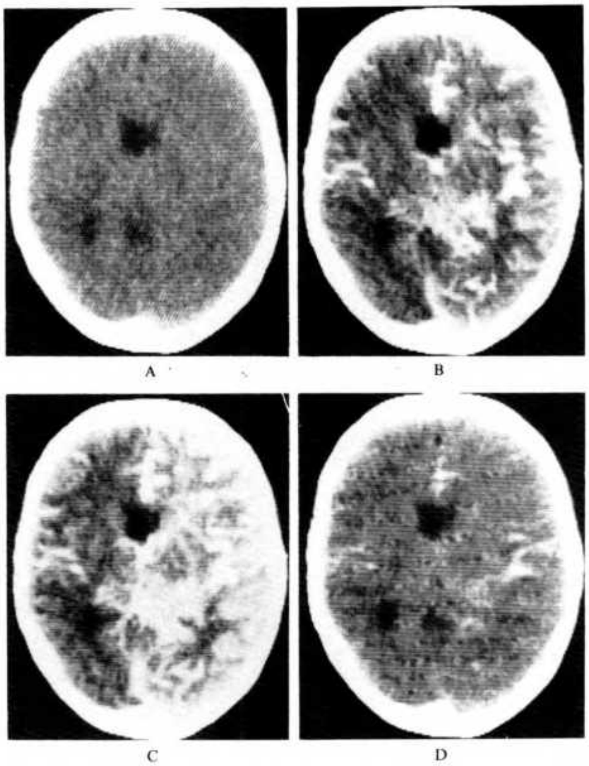


FIG. 5.

Dynamic CT images after bolus injection of contrast medium, at (A) 0 s, (B) 8 s, (C) 10 s and (D) 18 s. Enhancement of the right hemisphere in the arterial phase reflected the total arterial ectasia.

DISCUSSION

From the pathogenic point of view, it would appear that the majority of cases with arterial ectasia have associated atheroma (Boeri & Passerini, 1964; Hilton & Hoyt, 1966; Banna & Romeo, 1979; Goldstein & Tibbs, 1981). However, ectasia may occur without atheroma (Greitz & Lofstedt, 1954; Hulten-Gyllensten et al, 1959; Sacks & Lindenburg, 1969; Wallace & Jaffe, 1967; Eldevik & Gabrielsen, 1975; Oki et al, 1979; Mori, 1985; Tsukamoto et al, 1985). Sacks and Lindenburg (1969) reported a case of arterial ectasia in a 2-year-old child strongly suggesting a congenital aetiology. Arterial hypertension also appears to be a common feature of this disease (Greitz & Lofstedt, 1954; Hulten-Gyllensten et al, 1959; Sacks & Lindenburg, 1969; Rozario et al, 1978; Goldstein & Tibbs, 1981; Yu et al, 1982; Van Tassel & Gammal, 1985).

Loss of the elastic membrane with hyaline degeneration of the muscular layers was a common finding in the previous autopsy series (Greitz & Lofstedt, 1954; Hulten-Gyllensten et al, 1959; Sacks & Lindenburg, 1969; Oki et al, 1979).

TABLE I

SUMMARY OF CASES WITH CEREBRAL ARTERIAL ECTASIA REPORTED IN THE LITERATURE

Reference	No. of cases	Sex M : F	Age Mean (range)	Aetiology of arterial ectasia
Greitz & Lofstedt (1954)	5	5 : 0	(52–62)	arteriosclerosis or other
Hulten-Gyllensten et al (1958)	19	18 : 1	61(51–70)	arteriosclerosis or other
Bladin & Donnan (1963)	1	1 · 0	52	not described
Boeri & Passerini (1964)	10	7 . 3	(36–68)	arteriosclerosis?
Scott & Stauffer (1964)	1	1 · 0	44	not described
Hilton & Hoyt (1966)	1	1 · 0	68	arteriosclerosis
Wallace & Jaffe (1967)	1	1 . 0	54	congenital
Sacks & Lindenburg (1969)	34	?	(2–?)	congenital
Eldevik & Gabrielson (1975)	2	2 : 0	54(51,56)	congenital?
Peterson et al (1977)	4	3 · 1	60(50–70)	arteriosclerosis?
Scotti et al (1978)	1	1 0	63	not described
Rozario et al (1978)	1	1 · 0	57	not described
Oki et al (1979)	1	1 0	65	arteriosclerosis or other
Banna & Romeo (1979)	2	1 : 1	60(57,63)	arteriosclerosis?
Miner et al (1980)	1	0 : 1	44	congenital?
Goldstein & Tibbs (1981)	1	0 : 1	40	arteriosclerosis?
Yu et al (1982)	31	26 : 5	(43–73)	arteriosclerosis?
Tsukamoto et al (1985)	1	0 · 1	37	congenital?
Yamada et al (1985)	2	0 . 2	29(17,40)	not described
Van Tassel & Gammal (1985)	1	1 : 0	49	not described
Araki et al (present report)	1	0 · 1	23	congenital?

We suggest that there are two possible independent causes of arterial ectasia, namely arteriosclerosis and congenital malformation. We accordingly divided the previously reported cases into these two groups (Table I).

In the arteriosclerosis group, arterial ectasia appears in an older age group (40–70 years), and more commonly in males. In the congenital group, most patients are under 40 years old and females are affected more frequently than males. Unlike the first group, distal branches of the cerebral arteries are occasionally involved but irregularity of the arterial wall, indicating arteriosclerotic change, is not a feature in this group (Table II).

Megalencephaly is defined as an increase in the volume of the brain parenchyma and classified as one type of macrocephaly. It is of two types: anatomical megalencephaly, caused by increase in the size and number of neurons, and metabolic megalencephaly, caused by accumulation of abnormal material among the neurons due to intrinsic brain disease (Salmon & Flanigan, 1964; DeMyer, 1972; Miner et al, 1980). This case is in the former group, having no clinical or neuroradiological sign of metabolic disease. Only two cases of unilateral megalencephaly have been previously reported (Davis & Nelson, 1961, Laurence, 1964; Dom & Brucher, 1969; Bignami et al, 1968; Townsend et al, 1975). The authors, however, did not comment on the angiographic findings of their cases.

This patient is the first to demonstrate hemicerebral

TABLE II

CONGENITAL ARTERIAL ECTASIA

	Age, sex	Hypertension	Circulation time	Involved cerebral artery						
				VA	BA	ICA	ACA	MCA	PCA	others
Hulten-Gyllensten et al (1959)	62,M	+			+	++	–	–	–	
	56,F	+			+	++	–	–	–	
Wallace & Jaffe (1966)	54,M			+	+	++	–	+	–	Aneurysm
Sacks & Lindenburg (1969)	35,F	+		++	+	–	–	+	+	Aneurysm
	2	–					+			
Oki et al (1979)	65,M	+		++	+	++	+	+	+	
Yamada et al (1985)	17,F					+	+			Moyamoya
	40,F					+	+			Moyamoya
Tsukamoto et al (1985)	37,F			–	–	–	+	–	–	
Araki et al (present report)	23,F	–	Normal	–	–	–	+++	+++	+++	

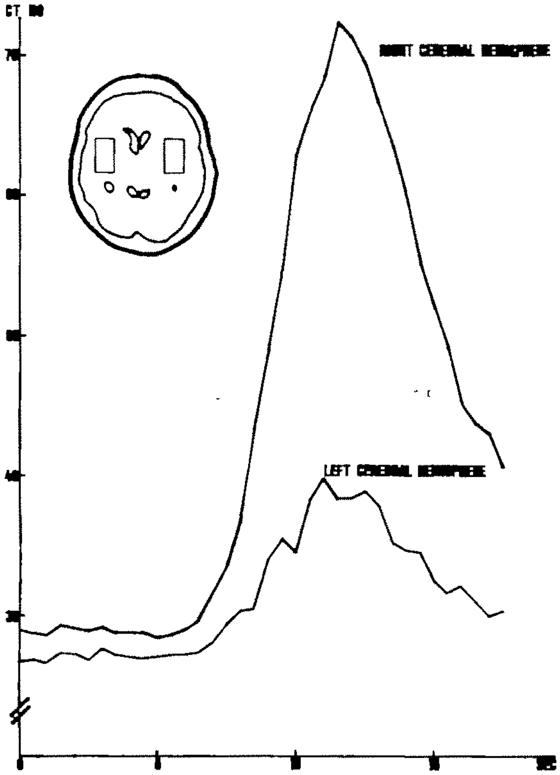


FIG. 6.

Dynamic dilution curves for both hemispheres. The height of the peak of the curve for the right hemisphere is abnormal. However, there was no phase difference between the two curves.

arterial ectasia complicating unilateral megalencephaly, although the association between the two pathological conditions remains controversial.

Hulten-Gyllensten et al (1959) said that the cerebral circulation time was found to be definitely prolonged in all of their three cases of arterial ectasia, determined both by serial angiography and by injection of radionuclides On the other hand, our case showed an increased circulation volume without prolonged circulation time in the affected hemisphere, presumably resulting from the increased demand for blood supply by the megalencephaly.

Although histopathological confirmation is lacking, we feel that the pathogenesis of our case is congenital, from its clinical picture and neuroradiological findings.

In the differential diagnosis, other conditions causing megalencephaly, such as achondroplasia, neurofibromatosis, tuberous sclerosis (anatomical megalencephaly), as well as the gangliosidoses, mucopolysaccharidoses, sulfatidoses etc. (metabolic megalencepaly), should be considered. Some blood vessel hamartomas, such as capillary telangiectasis and arteriovenous malformation, should also be considered. However, the neuroradiological findings in our case are so characteristic as to rule out these diseases.

ACKNOWLEDGEMENT

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Sialosis: diagnosis by computed tomography

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Sialosis, or asymptomatic parotid gland enlargement, is the term used to describe a non-inflammatory, non-neoplastic, chronic or recurrent, bilateral enlargement of the salivary glands (Mason & Chisholm, 1975a). Previously, diagnosis of this condition has been based on characteristic histological features of biopsy specimens from the enlarged glands. We report a case in which a diagnosis of sialosis was made on the basis of the appearance of the parotid glands as demonstrated by computed tomography (CT).

Case Report

A 63-year-old woman complained of gradual, painless enlargement of the left parotid gland of 7 months' duration The only relevant past medical history was of a partial thyroidectomy 20 years previously She was currently being treated with a thiazide diuretic for hypertension. Physical examination revealed marked bilateral enlargement of the parotid glands, the glands being firm to palpation. No other abnormality was found.

Thyroid function tests revealed borderline hypothyroidism. Other haematological and biochemical studies, including liver function tests, were normal. Left parotid sialography was performed and this demonstrated sparse ducts of small diameter which were slightly separated but with no evidence of a discrete space-occupying lesion (Fig. 1) Computed tomography confirmed the marked enlargement of both parotid glands; the submandibular and sublingual glands were normal. The attenuation coefficient of the parotid glands was equivalent to fat (−55 HU) and much lower than the normal range for parotid-gland parenchyma of −25 to 10 HU (Bryan et al, 1982) Prominent septa of soft-tissue density were seen within the gland parenchyma (Fig 2)

On the basis of the appearances on CT, a diagnosis of sialosis was made The patient has been placed on thyroxine but no other treatment has been instituted. Her clinical condition has remained unchanged for 1 year.

Discussion

Sialosis has a predilection for the parotid glands and women are more commonly affected than men. The disorder is of unknown aetiology but occurs most commonly in association with hormonal disturbances (particularly thyroid, ovarian and pancreatic dysfunction), malnutrition, liver cirrhosis and chronic alcoholism (Mason & Chisholm, 1975a). Borderline hypothyroidism could be a contributory factor in the present case. Many drugs have also been incriminated as the cause of sialosis including phenylbutazone, iodides, ganglion-blocking agents, and adrenergic and cholinergic drugs (Rabinov et al, 1984).

A diagnosis of sialosis was made in this patient on the basis of the clinical findings and the appearances of the CT scan. Glandular enlargement and sparse peripheral ducts are sialographic features suggestive of sialosis but they may be mimicked by diffuse infiltrative processes such as granulomatous diseases and the lymphomas (Som et al, 1981). The features of sialosis on CT are more specific and correlate with the histological findings (Rabinov et al, 1984). Initially,

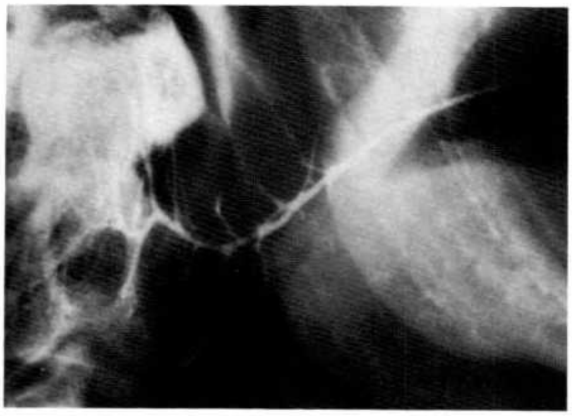

FIG. 1.

Lateral view of left parotid sialogram demonstrating sparse ducts of small diameter with generalised separation of the ductal branches.

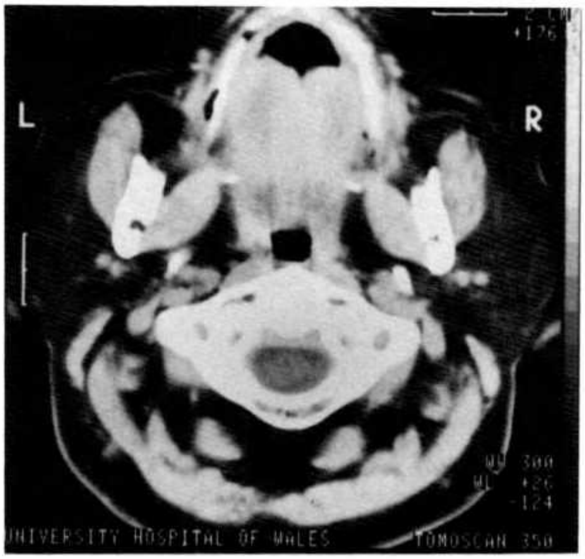

FIG. 2.

Axial CT scan through the parotid glands showing marked bilateral glandular enlargement. The attenuation coefficient of the glands is equivalent to fat and prominent soft-tissue septa are present.

hypertrophy of serous cells occurs with oedema of supporting interstitial tissues and atrophy of striated ducts. At this stage the parotid glands will appear diffusely enlarged on CT but of similar density to normal gland parenchyma. As the disease progresses, fatty replacement of the gland occurs with fibrosis of the interlobular septa (Batsakis, 1979). The attenuation coefficient of the gland decreases, approaching that of fat, with prominent septa of soft-tissue density interspersed throughout the gland. These appearances are highly suggestive of sialosis. The main differential diagnosis is that of age-related changes in the salivary glands. Autopsy studies have shown progressive replacement of salivary gland parenchyma by fat with increasing age (Waterhouse et al, 1973) and salivary gland enlargement has been reported to occur in the elderly (Mason & Chisholm, 1975b). However, the marked enlargement and almost total replacement of the glandular substance by fat, as in the present case, is diagnostic of sialosis. Lesser degrees of enlargement and fatty accumulation in an elderly patient, lacking a predisposing factor for sialosis, is more suggestive of an age-related change.

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Case reports

Multiple ileal carcinoid tumours

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Primary ileal carcinoid tumours frequently escape radiological detection: two reasons for this are their small size and their submucosal location (Hermanutz et al, 1974; Balthazar, 1978). We have recently reported the radiological appearances of primary ileal carcinoid tumours as shown by the small bowel enema (Jeffree et al, 1984). Ileal carcinoid tumours are multiple in approximately one-third of cases. Multiple primaries are only rarely detected on barium studies and we can find no cases in the radiological literature where multiple ileal primary carcinoids were clearly shown. We report a patient with the carcinoid syndrome in whom four primary, submucosal, ileal carcinoid tumours were shown by the small bowel enema.

CASE REPORT

A 47-year-old woman presented with a 5-month history of malaise, diarrhoea, weight loss, occasional flushing and weakness. On examination she had violaceous facial discolora-

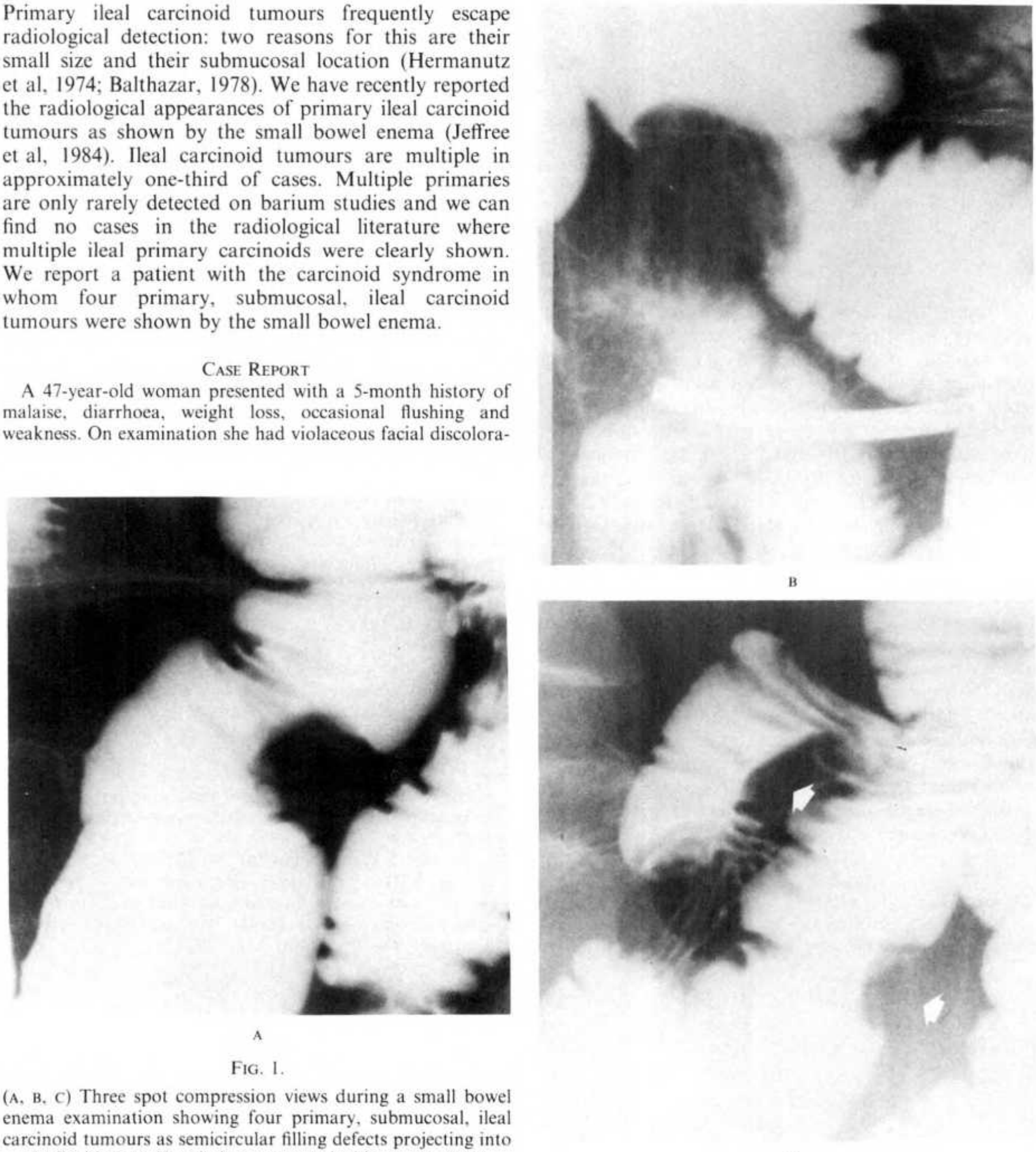

FIG. 1.

(A, B, C) Three spot compression views during a small bowel enema examination showing four primary, submucosal, ileal carcinoid tumours as semicircular filling defects projecting into the ileal lumen. Two lesions are seen in Fig. 1C (arrows).

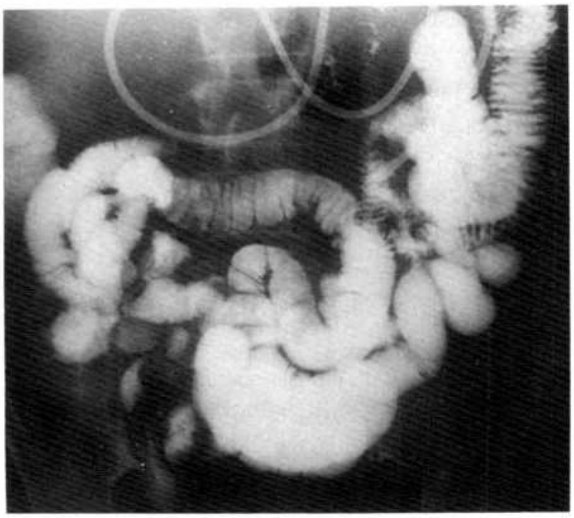

FIG. 2.

A general view of the small bowel enema examination demonstrating how difficult it is to see the carcinoid tumours without the use of compression.

tion, cardiomegaly, an enlarged, irregular liver, moderate splenomegaly and ankle oedema. Pulse and blood pressure were normal. Her 24 h urinary 5-hydroxyindole acetic acid excretion was greatly raised at 750 mg in 24 h (normal 25 mg per 24 h). A diagnosis was made of carcinoid syndrome with hepatic metastases and this was confirmed by needle biopsy of the liver. Small bowel enema examination showed four primary, submucosal, ileal carcinoid tumours (Fig. 1). A laparotomy was performed with the intention of enucleating the hepatic metastases but these proved too extensive for the procedure to be worthwhile. She was treated medically and died 13 months after presentation. Post-mortem examination was not performed.

DISCUSSION

Multiple primary ileal carcinoid tumours are well recognised (Hudson & Margulis, 1964; Schlangen, 1976; Grahame-Smith, 1977) and occur in approximately one-third of cases (Bancks et al, 1975; Balthazar, 1978). We have not, so far, seen a convincing demonstration of multiple ileal carcinoid tumours in the radiological literature.

Numerous radiological signs of ileal carcinoid tumours have been described. The most frequently encountered are intraluminal filling defects, ileal narrowing, separation of ileal loops and partial ileal obstruction (Jeffree et al, 1984). Sharp angulation or kinking of an ileal loop is characteristic but occurs less frequently.

The four lesions demonstrated in the present case were all discrete, submucosal, ileal filling defects appearing as broad-based semicircular impressions, 1–3 cm in diameter, projecting into the ileal lumen from one wall. They were not readily detectable on the large radiograph (Fig. 2) but were clearly demonstrated on spot-compression views (Fig. 1). Evidence would suggest that the small bowel enema (enteroclysis, barium infusion examination) is more accurate in the detection of primary ileal carcinoid tumours (Jeffree et al, 1984; Schlangen, 1976) because it produces greater intestinal distension than the barium follow-through examination. Fluoroscopy during the procedure increases the likelihood of observing any lesion which may be present and the value of compression in displacing overlapping intestinal loops away from the loop under examination is emphasised.

Carcinoid tumours should always be considered when multiple polypoid lesions are seen in the ileum.

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Case reports

Barium embolisation during barium enema examination: a report of a case and a review of the literature

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Barium embolisation is a rare complication of barium enema examination but carries a mortality of greater than 50%. Fifteen cases have been reported previously. We describe a further case in which the patient survived after emergency subtotal colectomy. The factors which are thought to predispose to this complication are discussed.

CASE REPORT

A 38-year-old woman presented with a severe exacerbation of Crohn's colitis. Since the initial diagnosis, she had been asymptomatic for 5 years on a maintenance dose of sulphasalazine, but she now complained of 2 months' watery diarrhoea and abdominal pain. She reported frequent fevers during this time but these were thought to be secondary to recurrent urinary tract infections because of an indwelling urinary catheter, necessitated by multiple sclerosis since the age of 15 years. She was pale but apyrexial and abdominal and sigmoidoscopic examinations were normal. Laboratory examinations revealed a haemoglobin of 7.7 g/dl and an erythrocyte sedimentation rate of 110 in the first hour. White cell count, urea, electrolytes and liver function tests were normal. *Escherichia coli* were grown from urine but nothing from stool or blood.

A barium enema was performed using a Foley catheter inflated with 30 ml of air. Severe Crohn's disease of the colon was demonstrated with deep penetrating ulcers. During this examination a fistula was noted between the splenic flexure and the region of the spleen. Barium was seen to enter the splenic veins. The examination was immediately terminated and the barium and air evacuated, but at fluoroscopy barium emboli were observed passing along the splenic and portal veins and lodging in the intrahepatic branches of the right portal vein (Figs 1, 2).

Despite treatment with intravenous antibiotics the patient became shocked 90 min after the examination. At emergency laparotomy the colon was grossly diseased. No communication could be identified between the bowel lumen and the normal spleen or any blood vessel. A subtotal colectomy was performed and an ileostomy fashioned. There was no evidence of sepsis post-operatively, antibiotics being discontinued after 7 days. The patient remains well 6 months later, although the intrahepatic barium aggregates are unchanged.

DISCUSSION

The commonest complication of a barium enema examination is perforation of the colon which, at a conservative estimate, occurs once in every 2500 examinations and carries a 50% mortality rate (Essinger & Aquet, 1984). Barium embolisation is less frequent but carries an even higher mortality. The site of intravasation and its venous drainage determine whether barium embolises to the systemic or portal circulation. The inferior and middle haemorrhoidal veins drain the distal rectum into the systemic circulation. The superior haemorrhoidal veins and the inferior mesenteric vein drain the remaining rectum and the sigmoid colon into the portal system. The colon proximal to the splenic flexure drains into the portal circulation through the superior mesenteric vein.

In Table I we set out the clinical findings and site of embolisation of the 16 cases reported, including our own. The type of catheter used during the barium enema is also listed. Nine of the 16 patients died: an overall mortality of 56%. Embolisation into the systemic circulation occurred in 10 patients, eight of whom died (80% mortality). There was only one death among the six patients in whom embolisation was into the portal system.

The discrepancy in survival rates between embolisation into the systemic and portal circulations may be explained in part by the observation that embolisation into the systemic circulation occurred in elderly patients (average age 72 years), while the average age in cases of portal embolisation was 43 years. However, the amount

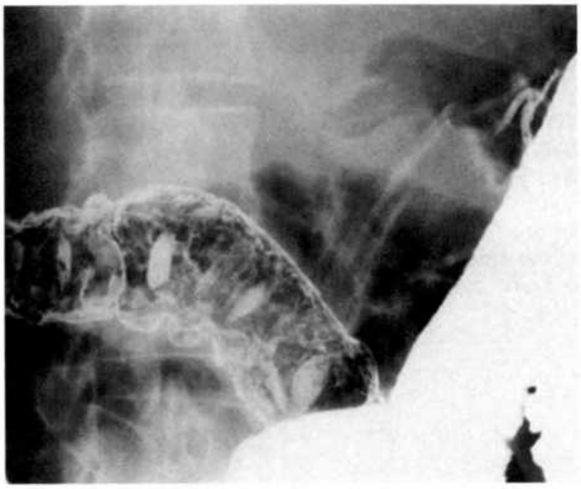

FIG. 1.

Barium enema showing severe Crohn's disease with deep penetrating ulcers in the transverse colon. Embolisation of barium into the splenic vein tributaries and into the main splenic vein is shown.

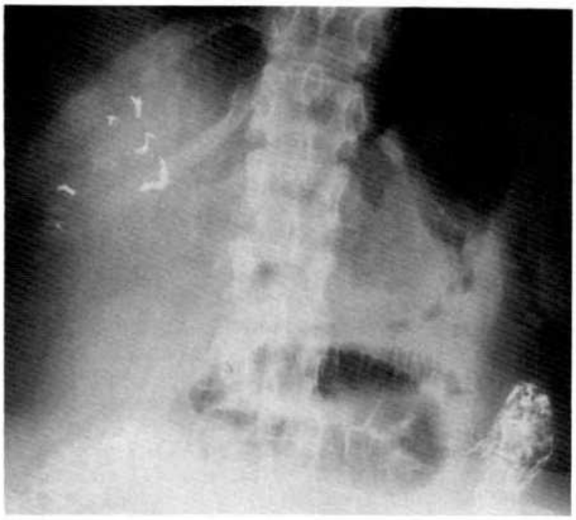

FIG. 2.

Barium emboli seen in the intrahepatic branches of the right portal vein after termination of the examination.

of barium which enters the circulation is probably an equally important determinant of outcome. Where embolisation is to the systemic circulation, large volumes of barium are often involved. Rosenberg and Fine (1959) illustrated a massive quantity of barium in the right side of the heart and in the pulmonary circulation. Frecker (1968) reported that the speed with which barium flowed into the venous system was astonishing. In contrast, when embolisation is into the portal circulation, probably considerably less barium enters the venous system. Archer and Freeman (1981) estimate that in their case a maximum of 5 ml of barium entered the circulation. In our case, judging by the deposits in the liver, less than 5 ml of barium was intravasated. Perhaps, too, the liver acts as a filter, entrapping the barium and associated faeces and bacteria, thereby limiting the potential toxicity.

Barium embolisation may be more likely where colonic mucosal integrity is compromised. In our case there was extensive Crohn's colitis. Three of the 16 patients suffered from ulcerative colitis and in four cases diverticular disease was present. Portal venous gas in the liver has been reported following both single- and double-contrast barium enemas in patients with ulcerative and Crohn's colitis (Gelfand, 1980; Bull & Kaye, 1985) and in diverticular disease (Stein et al, 1983). This has been described as a harmless clinical sign (Bull & Kaye, 1985) but in at least two cases described by Gelfand (1980) there was associated shock of sufficient severity to require intravenous fluids and antibiotics.

Transient bacteraemia commonly follows sigmoidoscopy or barium enema in patients with inflammatory bowel disease (Fraser & Findlay, 1976). It is likely that this is due to small amounts of faecal-contaminated gas entering the venous system during these procedures and is rarely of clinical importance. Colonoscopy does not appear to carry a higher risk of bacteraemia than barium enema or sigmoidoscopy, even if biopsy is included (Kumar et al, 1982).

A balloon-type catheter was used in 12 of the 16 cases. In three reports the type of catheter was not stated. Juler et al (1976) suggest that the close association of embolisation with the use of a balloon catheter is more than just coincidence. The close proximity of the haemorrhoidal venous plexus to the rectal mucosa may predispose to embolisation. The

TABLE I

PRINCIPAL FEATURES OF 16 RECORDED CASES OF BARIUM EMBOLISATION DURING BARIUM ENEMA

Reference	Age (years)	Sex	Type of catheter	Colonic pathology	Embolus		Outcome
					Origin	Site	
Isaacs et al, 1950	25	F	Not stated	Ulcerative colitis	Transverse colon	Portal	Survived
Roman et al, 1952	78	F	Balloon	None found	Rectum	Systemic	Died
Rosenberg and Fine, 1959	73	F	Balloon	None found	Rectum	Systemic	Died
Truemner et al, 1960	76	F	Balloon	None found	Rectum	Systemic	Died
Zatkin and Irwin, 1964	65	F	Balloon	None found	Vagina	Systemic	Survived
Geipel, 1967	77	F	Not stated	None found	Vagina	Systemic	Died
Frecker, 1968	81	F	Balloon	None found	Rectum	Systemic	Died
Noveroske, 1966	72	F	Balloon	None found	Rectum	Systemic	Died
Nordahl et al, 1973	39	M	Balloon	Diverticular disease	Sigmoid colon	Portal	Survived
Cove and Snyder, 1974	64	F	Balloon	Diverticular disease	Sigmoid colon	Systemic	Died
Salvo et al, 1976	36	F	Balloon	Ulcerative colitis	Transverse colon	Portal	Died
Juler et al, 1976	35	M	Balloon	Diverticular disease	Sigmoid colon	Portal	Survived
Archer and Freeman, 1981	86	M	Not balloon	Carcinoma	Colostomy	Portal	Survived
Tsoutsanis, 1981	67	M	Not stated	Ulcerative colitis	Rectum	Systemic	Died
Blom et al, 1983	73	F	Balloon	Diverticular disease	Rectum	Systemic	Survived
Present case	38	F	Balloon	Crohn's colitis	Transverse colon	Portal	Survived

elderly are more at risk because of thinning and diminishing elasticity of the rectal wall with age. Where embolisation was from the rectum or vagina into the systemic circulation the average age of the patient was 72 years. In most studies balloon catheters, when used, have been inflated with between 70 ml and 150 ml of air (Frecker, 1968). We routinely use a balloon catheter but do not inflate it with more than 50 ml of air. We feel that the very small risk of perforation or embolisation is far outweighed by the advantage of obtaining a satisfactory examination in patients with poor sphincter control. We do not think that in our case the balloon catheter played any part in the embolisation of barium from the splenic flexure.

In summary, of the 16 recorded cases of barium embolisation during barium enema examination, 10 were into the systemic and six into the portal circulation. Overall mortality was 56% but it was significantly higher in those cases with systemic embolisation. This increased mortality is probably related to the greater volume of barium which enters the circulation. In nearly every case a balloon-type catheter was used. It is suggested that care be exercised in the amount of air with which these catheters are distended, particularly in the elderly. Where embolisation does occur, partial colectomy may have a place in the patient's resuscitation.

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1987, *The British Journal of Radiology*, 60, 407–409

APRIL 1987

Case reports

Unilateral breast hyperplasia in pregnancy simulating neoplasm

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Moderate bilateral enlargement of the breasts is a normal finding during pregnancy and lactation. There is a continuity from this physiological hypertrophy to a massive breast hyperplasia or gigantomastia complicating pregnancy, occurring in about one in 28 000 births (Lewison et al, 1960). The physiological breast hypertrophy of pregnancy as well as the rare gigantomastia are bilateral in the vast majority of cases. The presence of tumour should always be suspected in cases of unilateral breast enlargement. We present what we believe is the first description of a massive unilateral breast hyperplasia in pregnancy simulating neoplasm on mammography and ultrasonography.

CASE REPORT

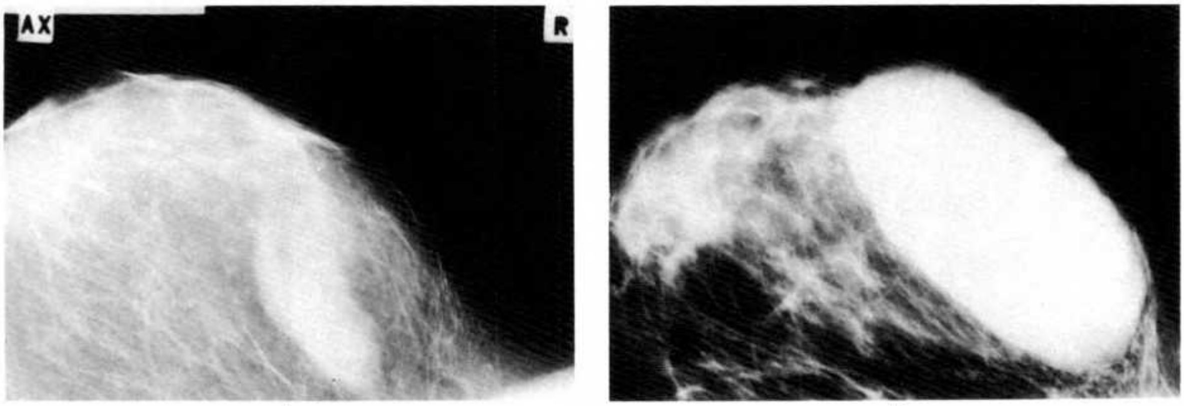
A 23-year-old woman with two children from separate pregnancies was referred to the department of radiology for mammography because of cancerophobia. Both her grandmother and mother had died of breast cancer. The breasts had been unremarkable in her two previous pregnancies. An incision of a right-sided breast abscess had been performed 3 years previously. On physical examination, a scar and slight skin retraction was found in the upper outer quadrant of the right breast. No tumour could be palpated. Mammography performed on May 15, 1984, showed an oval density in the upper outer quadrant of the right breast consistent with a prominent axillary tail of the parenchyma and probably some contribution from scar tissue following the previous incision (Fig. 1A).

The patient was re-admitted for mammography 5 months later when she was 4 months pregnant. During the previous weeks she had noticed rapid enlargement of the right breast. On physical examination, a large, non-tender, soft mass was suspected in the upper outer quadrant. Mammography performed on October 10, 1984, revealed a large oval, well circumscribed, homogeneous density (Fig. 1B). The lesion obviously represented massive enlargement of the small density demonstrated 5 months earlier. On ultrasonography, the well circumscribed lesion had evenly distributed, fine, internal echoes (Fig. 2). An excision of the "tumour" was carried out because of the rapid enlargement. The post-operative course was uneventful.

Histological examination of the resected specimen, measuring 12 cm × 10 cm × 10 cm, revealed proliferation of the duct system and alveoli (Fig. 3A). The alveolar spaces were expanded, varying significantly in size (Fig. 3A). The alveoli were covered by a single layer of columnar cells with some myoepithelial cells at their periphery. The epithelial cells showed some cytoplasmic vacuolisation, suggesting secretory activity (Fig. 3B). The ducts were surrounded by stroma containing elastic fibres. The histology was consistent with breast tissue at 4–6 months' pregnancy.

DISCUSSION

The massive hyperplasia of the breasts may, as in our case, occur early in pregnancy (Burslem & Dewhurst, 1952; Williams, 1957; Blaydes & Kinnebrew, 1958). The clinical course is characterised by tenderness and rapid increase in breast size. The growth of the breasts is



A

B

FIG. 1.

(A) Oblique mammogram of the right breast showing a density in the upper outer quadrant. (B) Oblique mammogram 5 months later showing a large, ovoid, well circumscribed, homogeneous density.

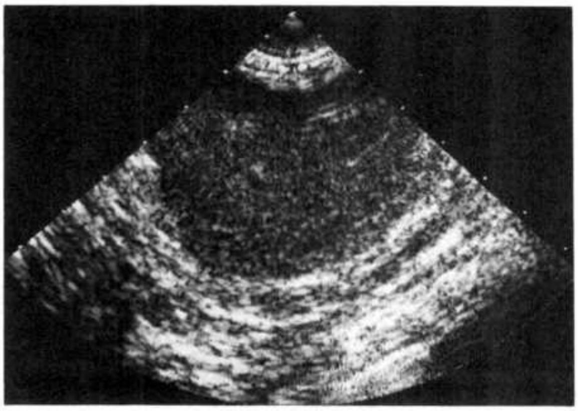


FIG. 2.
Sonogram showing a large solid breast mass containing evenly distributed, fine, internal echoes.

probably the result of hormone stimulation (Lewison et al, 1960), but no distinct hormonal cause has been revealed. It is of interest that the condition may occur in multiparous women who have had no such problem in previous pregnancies (Blaydes & Kinnebrew, 1958; Bhattacharaya, 1983). The diagnosis is based on history and physical examination in cases of bilateral breast hypertrophy or bilateral hypertrophic axillary tails. In the rare cases of unilateral breast hypertrophy, however, the presence of tumour should always be suspected. The diagnosis of breast carcinoma, the most important differential diagnosis in unilateral breast hyperplasia, is difficult in the pregnant patient. Patients with breast cancer diagnosed during pregnancy or lactation are often in an advanced stage of the disease (Hornstein et al, 1982; King et al, 1985). This delayed diagnosis of breast cancer during pregnancy may be partly explained by the difficulties in palpating the enlarged breast, and partly because of an over-cautious

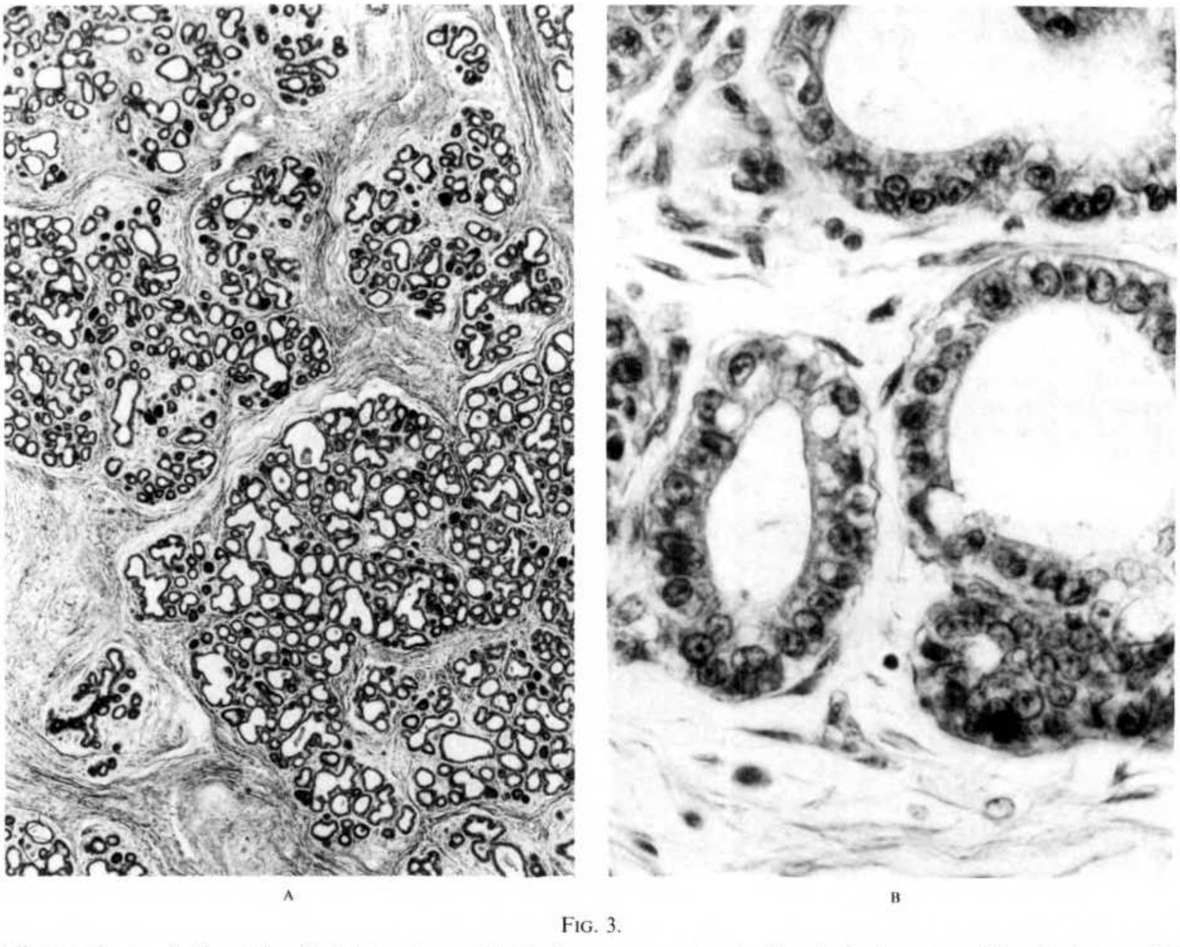


FIG. 3.
Microscopic examination: (A) epithelial structures with alveolar spaces varying significantly in size, compatible with 4–6 months' pregnancy (H&E, ×10) and (B) the alveoli lined by a single layer of epithelial cells occasionally containing prominent vacuoles (H&E, ×480).

attitude towards the pregnant woman (Hornstein et al, 1982). As a result, diagnostic procedures, including mammography and biopsies, are delayed.

The differential diagnosis of the mammographic and ultrasonic findings (Figs 1B, 2) include fibroadenoma, cystosarcoma phylloides and carcinoma. The large, oval, well circumscribed, homogeneous density (Fig. 1B) has nothing in common with the diffuse increased density, blurring and overall fluffiness with loss of definition of the parenchyma usually seen on mammograms during pregnancy. The soft, ill-defined lesion on physical examination was less compatible with a fibroadenoma. The ovoid configuration of the density on mammography was less compatible with a carcinoma. The soft non-tender mass on physical examination, in combination with the mammographic and ultrasonic findings, favoured a diagnosis of cystosarcoma phylloides. Characteristic findings of cystosarcoma phylloides, however, include a lobulated appearance of homogeneous density on mammography and the presence of elongated fluid-filled cystic spaces on ultrasonography (Cole-Beuglet et al, 1983). Microscopically, the features of pregnancy may be quite similar to the histological findings in lactating adenomas. Lactating adenoma is a rare, benign tumour found during pregnancy and lactation (Hertel et al, 1976) which maintains most of the ultrastructural features of lactating breasts. The "tumour" in our case was not well demarcated on histological examination and the ductules more varied in size and separated by more connective tissue than in lactating adenoma (Figs 3A, B). In addition, the elastin staining was positive in our case. The ducts were surrounded by stroma containing well organised elastic fibres. Furthermore, lactating adenomas are usually rather small lesions varying from 1.0 cm to 3.5 cm in diameter (Hertel et al, 1976).

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Book reviews

Care of the Patient in Diagnostic Radiography, 6th edit. By D. N. Chesney and M. O. Chesney, pp. xii+368, 1986 (Blackwell Scientific, Oxford), £9.80
ISBN 0–632–01558–6

This is the sixth edition of a book first published in 1962, and aimed at radiographers who at that time had a 2-year training course. Since then the course has been extended and the syllabus modified. How well has the latest edition kept up with the times?

The authors are two well known radiographers who have attempted to explain to young radiographers their duties in relation to the care of patients in the department of radiography, and at the same time to teach them biology and basic medicine, together with nursing procedures. The headings of the 20 chapters give a measure of the scope: features of general patient care; drugs in the X-ray department; sterilisation and sterile techniques; preparation of the patient; a series of chapters on the gastrointestinal, renal and biliary tracts, with others on various radiological procedures; nursing procedures; first aid in the department; medico-legal aspects; and others. All of these are well intentioned, but the attempt to be all-inclusive has meant that important details are lost in some areas, and that others are too superficial. On Page 211 the trocar inserted into the top of an intravenous administration set is not labelled, and this might result in a student losing an examination mark. The section on the cardiovascular system starts with the statement that the system is one of closed pipes, which seems to be aimed at a basic level, and yet the next section is on electrocardiography and contains a completely unexplained trace of a 12-lead recording. A little later come three pages on "how to give a bed-pan" in which the main points are obscured in waffle. The style of writing is sometimes strange, as in the section on drugs where it is said that "Controlled drugs are issued to 'the man in the street' only on the written prescription of a doctor"—are we talking about drug-addicts? The index is also idiosyncratic: "ERCP" is between "expired air" and "explosion risk", "ten-day rule" has two entries and "thermometer" comes between "test dose" (first) and "telepaque"

Although there is a real need for a book covering this area and this is the only one available, it is showing its age, is difficult to read, is incomplete and will not fully meet the requirements of the modern student radiographer.

C. Tharby

Back Pain. Methods for Clinical Investigation and Assessment. Ed. by D. W. L. Hukins and R. C. Mulholland, pp xiv+167, 1986 (Blackwell Scientific Publications, Oxford), £25.00.
ISBN 0–7190–2311–4

"The Society for Back Pain Research meets twice a year so that its members may present and discuss their research." Thus opens the Preface to this book. It continues, "Investigation and assessment of Back Pain is an area where considerable advances have been made in the last few years. Its interdisciplinary nature made the subject more appropriate for a Meeting of the Society, and for publication of the proceedings."

The book is, thus, a collection of abstracts or mini-papers covering a wide spectrum indeed. It ranges from moire topography to quantitive magnetic resonance. In all, 15 presentations are included with good reproduction of images from the various imaging techniques discussed, a few references and pertinent discussion points from the audience.

Can one recommend it? Always when reading the publication of proceedings, one inevitably feels as though one is eavesdropping on a private club. The obviously enthusiastic and intense interest of the participants shines through. The messages in each communication are directed to the fellow members of the Society to provoke thought, comment and self-education. Hence, the book does not attempt to proselytise or to advance the understanding of back pain for ordinary mortals. Consequently, it does not seem to hold appeal for the average radiologist, orthopaedic surgeon or rheumatologist except, perhaps, for those departments which have a major interest in spinal disease. In such departments, however, it may also be argued that the staff are well aware of the messages contained within this book, if indeed they hadn't actually written them!

Iain Watt

1987, *The British Journal of Radiology*, *60*, 411–413

Case of the month

Rounded opacity in a young man's chest

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(Received August 1986)

A 30-year-old man with a 12-year history of cigarette smoking was admitted with low-grade, remittent fever of 2 months' duration, recurrent haemoptysis and mild diffuse pain in the right hemithorax. During the last 2 months he had received broad-spectrum antibiotics, which did not change the course of the disease.

On admission, examination revealed a respiratory rate of 16 breaths/min and a temperature of 37.8°C. A few crepitations were audible in the right infrascapular region. The abdomen was soft and did not reveal any abnormality. White blood cell count was 9400/mm^3 with 60% neutrophils and 40% lymphocytes. Other routine biochemical investigations, including liver function tests, were within normal limits. The chest radiograph on admission showed a well defined, round, homogeneous opacity in the right lower zone with a normally placed right dome of the diaphragm (Fig. 1).

What are possible diagnoses and how would you proceed?

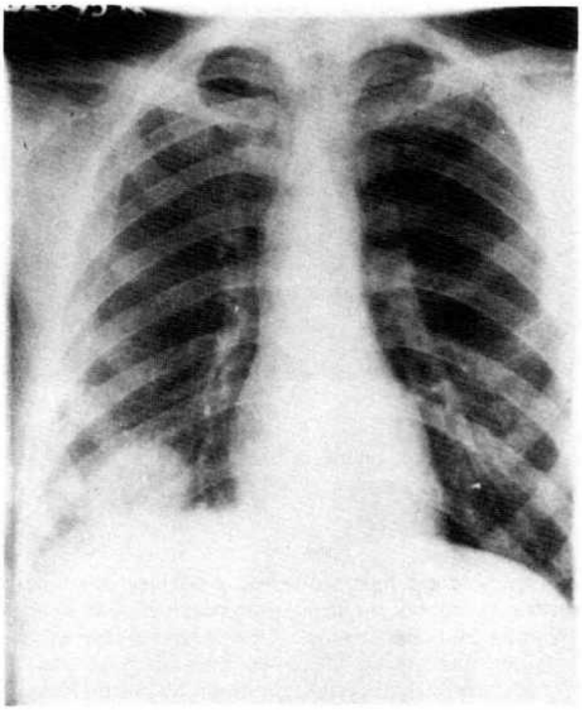
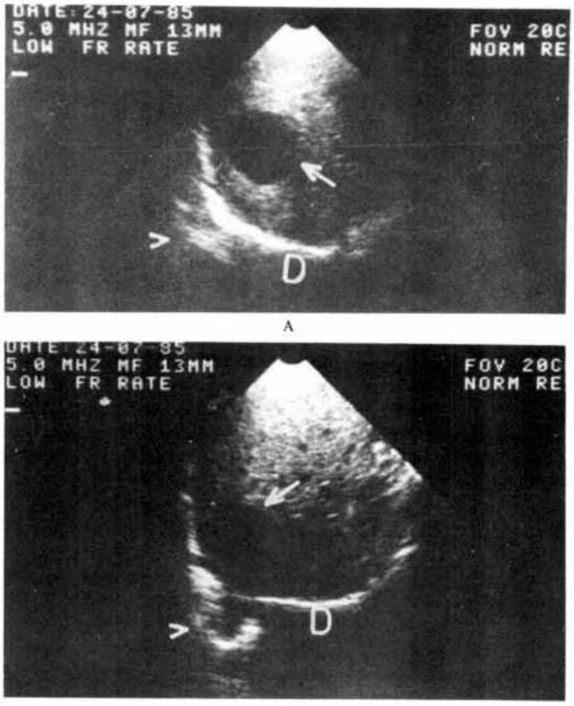


FIG. 1.

Chest radiograph on admission.



A

B

FIG. 2.

(A) Transverse and (B) longitudinal sonograms through the superior part of the liver.

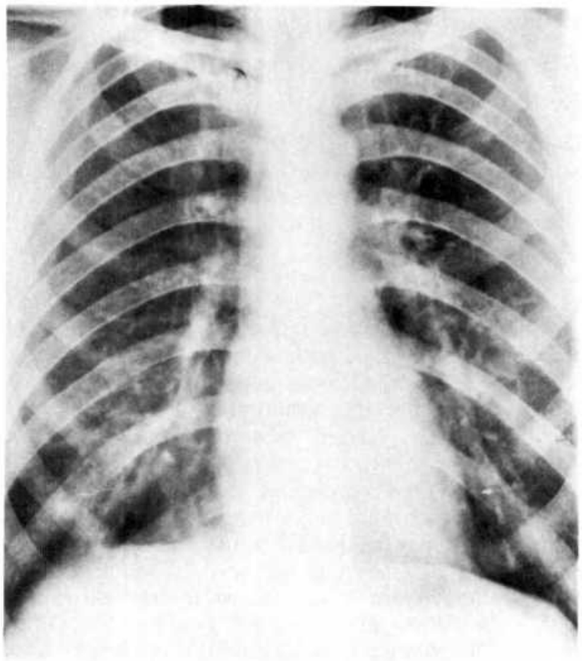


FIG. 3.

Chest radiograph after 2 weeks of anti-amoebic therapy.

The most common causes of a solitary pulmonary nodule in order of frequency are granulomas, malignant tumours and hamartomas. Less common causes are localised pneumonia, abscesses, hydatid cysts, pleural fibromas, bronchial cysts and arterio-venous malformations, with many other causes described (Higgins et al, 1975).

The discovery of an isolated opacity on a chest radiograph poses a number of problems for the radiologist.

Is it within the chest? In this case a lateral radiograph confirmed that it was in the lower lobe.

Are other lesions present? It is our practice to carry out real-time ultrasonography when possible and routinely to examine the upper abdominal organs in case relevant abnormalities are present. In this patient an anechoic, well defined lesion was seen in the posterosuperior part of the right lobe of the liver (Fig. 2), measuring 5.2 cm × 5.0 cm × 4.8 cm with posterior enhancement, and the lesion in the lung was also anechoic and situated close to the hepatic lesion.

Can a tissue diagnosis be obtained? Diagnostic needle aspiration from the hepatic lesion under ultrasound guidance revealed typical "anchovy sauce" material, diagnostic of an amoebic liver abscess, and suggesting that the pulmonary opacity was a secondary abscess. Stool and sputum examination, as well as pus from the liver, failed to show *Entamoeba histolytica*.

Treatment with intramuscular emetine hydrochloride for 10 days produced remission of symptoms after 5 days, with partial resolution of the opacity on the chest radiograph after 2 weeks (Fig. 3), and complete resolution after 4 weeks. The liver abscess had still not completely resolved after 4 weeks of treatment.

DISCUSSION

Amoebic lung abscess is an unusual cause of a rounded pulmonary opacity and is usually seen secondary to amoebic liver abscess (Wilson, 1971). The other thoracic complications of amoebic liver abscess include consolidation, rupture into the pleura or pericardium and broncho-biliary fistula (Wilson, 1971; Ibarra-Perez, 1981). Fine-needle aspiration biopsy is a simple and effective way of making a pathological diagnosis, when conventional radiology and bronchoscopy cannot help (Ikezoe et al, 1984).

Demonstration of vegetative *Entamoeba histolytica* in the sputum, pleural fluid or pus is the definitive proof of diagnosis, but this may not be found and the demonstration of "anchovy sauce"-like pus and the clinical response to emetine therapy is generally accepted as proof of the diagnosis (Pande & Srivastava, 1966).

In our patient the probable diagnosis was suggested by finding a lesion in the liver which had the same consistency as that in the lung, and the diagnosis was proved by aspiration from the liver of the typical "anchovy-sauce" pus, together with the patient's response to emetine. We consider that the upper abdomen should always be examined in patients having ultrasound of the chest.

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Short communication

Ultrasound examination of the paediatric "acute abdomen": preliminary findings

By * R. M. Mendelson, M.R.C.P., F.R.C.R. and D. R. M. Lindsell, F.R.C.R.

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(*Received June 1986 and in revised form August 1986*)

Acute abdominal pain is common in children and, although, over the age of 2 years, the commonest single cause is acute appendicitis, over 60% of patients admitted to hospital have non-surgical causes of their pain (Drake, 1980). Clinical differentiation, between appendicitis and the larger group of other causes which do not require operative treatment, is often difficult. Consequently, the negative laparotomy rate is high, at around 20%. Of the radiological procedures available, plain abdominal radiography is sometimes diagnostic but is not sensitive (Soter, 1973). Barium enema may be useful, but an abnormal examination is relatively non-specific (Ostreich et al, 1981; Fedyshin et al, 1984) and the procedure is upsetting for young children. Recently, ultrasound examination has been employed for surveying children with acute abdominal symptoms (Miller & Kemberling, 1984) and, specifically, in those with suspected appendicitis (Parulekar, 1983; Karstrup et al, 1986; Puylaert, 1986). Computed tomography has also been used but has the disadvantages of being less widely available and of employing ionising radiation.

We report our preliminary findings in a prospective study of real-time ultrasound in children presenting with an "acute abdomen".

MATERIAL AND METHODS

Twenty-four consecutive children aged 2–16 years (15 male, nine female), admitted to hospital with an "acute abdomen", were examined within 24 h of admission with a Toshiba linear-array real-time ultrasound machine fitted with a 5 MHz probe. In most cases ultrasound was performed immediately on admission. A general abdominal survey was followed by a detailed examination of the right iliac fossa (RIF). The ultrasound findings were reported to the admitting clinician but it was stressed that the decision whether to operate or request other investigations should not be made on the basis of the ultrasound result.

RESULTS

The suspected clinical diagnoses on admission are summarised in Table I. All but three patients had clinical features consistent with acute appendicitis or required exclusion of this diagnosis.

Table II summarises the diagnoses on discharge, and the numbers having positive ultrasound in each category. Of the two patients with suspected intestinal intussusception, ultrasound in one showed the typical concentric-ring appearance (Fig. 1), which was confirmed by barium enema, while the other was negative on ultrasound and barium enema.

The abnormalities seen on ultrasound in the 11 patients with confirmed acute appendicitis are detailed in Table III. The commonest finding (7/11) was thickening of the wall of more than one loop of bowel in the RIF (Fig. 2). In two patients, a few fluid-filled loops of bowel were identified in the RIF but without wall thickening and with normal peristalsis; this finding was regarded as normal. One of these patients subsequently proved to be in the non-surgical group; the other had equivocal appendicitis at operation (a "slightly pink appendix" macroscopically and "very early appendicitis" histologically). One other false negative ultrasound scan occurred: this, in retrospect, was due to a misinterpretation of the findings, an appendix mass being regarded as a faecal-loaded caecum (Fig. 3). One false positive ultrasound scan occurred in the non-surgical group when a single thickened loop of bowel was identified in the RIF.

TABLE I

CLINICAL DIAGNOSES ON ADMISSION

Acute appendicitis, mesenteric adenitis or appendix mass/abscess	21
Small-bowel obstruction	1
? Intussusception	2

DISCUSSION

Puylaert, using ultrasound during graded compression, has succeeded in visualising the inflamed appendix with a high degree of sensitivity. Recently Karstrup et al (1986) reported similar findings with ultrasound in a group of adults prior to appendicectomy, the abnormal appendix appearing as an echo-poor/echo-free lesion with lack of movement, rather than a "target" structure. They remark that the non-visualisation of

TABLE II

FINAL DIAGNOSES CORRELATED WITH ULTRASOUND RESULT

Diagnosis on discharge	Total	Abnormal ultrasound	Normal ultrasound
(a) Acute appendicitis with or without mass or abscess (confirmed by surgery)	11	9	2
(b) Settled on no treatment (mesenteric adenitis or no diagnosis reached)	7	1	6
(c) Intussusception	1	1	
(d) Small-bowel obstruction	1	1	
(e) Other diagnosis (one case each of pneumonia, urinary infection, constipation and enteritis)	4		4
Total	24	12	12

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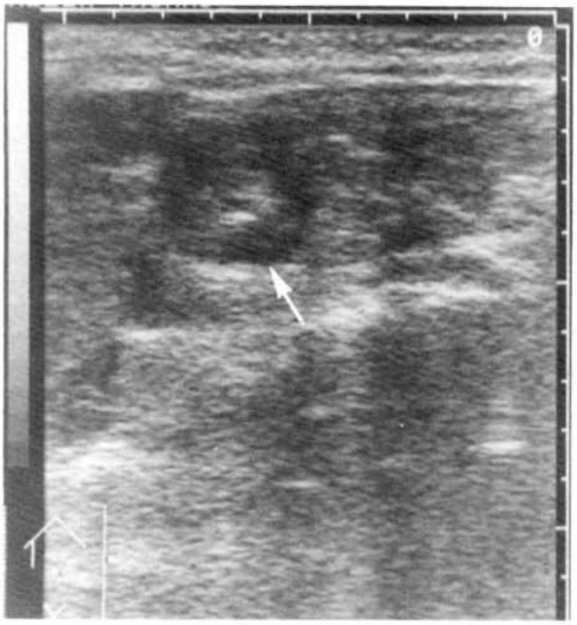

FIG. 1.

Concentric-ring appearance (arrowed) of an ileocolic intussusception seen transversely in the epigastrium.

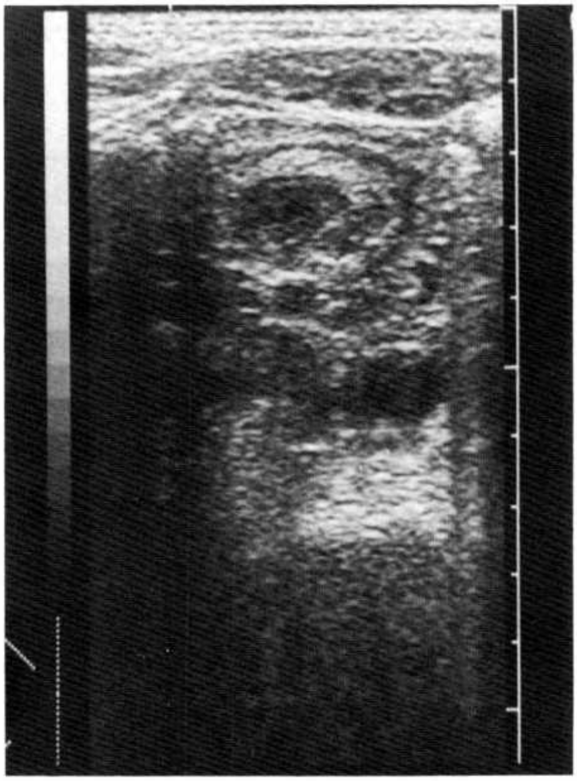

FIG. 3.

False negative ultrasound scan in a 14-year-old girl. Reported as faecal residue in the caecum. Subsequently, a complex appendix mass was found, with adherent loops of bowel.

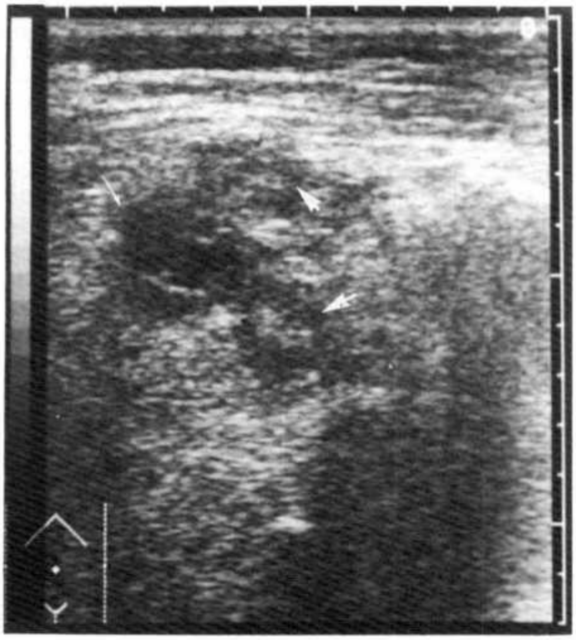

FIG. 2.

Right iliac fossa scan in a 9-year-old girl showing thickened loops of bowel (large arrows), and a complex inflammatory mass with abscess formation (small arrows) (confirmed surgically).

such a sonolucent lesion does not exclude appendicitis. In our small series of children presenting with acute abdominal pain we elicited a single "target" sign in only one patient, although it is possible that in some patients one of the thickened loops of bowel demonstrated was, in fact, the inflamed appendix. We have relied, instead, predominantly on the secondary and indirect signs of inflammation in the RIF. Although one would not expect, in this way, to distinguish acute appendicitis from acute ileitis, these latter patients are only a small group. In addition, ultrasound is able to identify those patients with an

TABLE III

FINDINGS ON ULTRASOUND IN 11 PATIENTS WITH APPENDICITIS

Localised ileus RIF (fluid-filled loops without peristalsis)	2
Mural thickening of loops of bowel in RIF + adherent loops	7
"Target sign" RIF	1
Abscess	3
Free fluid RIF	2
Small-bowel obstruction	1
Appendicolith	1
Normal	2*

Several patients had more than one ultrasound sign.
*Equivocal operative findings (1); mass in retrospect (1).

1987, *The British Journal of Radiology*, 60, 417–418 APRIL 1987

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Buscopan and glaucoma

THE EDITOR—SIR,

The use of Buscopan (hyoscine butylbromide, Boehringer Ingelheim) is routine in some radiological procedures, and prior to its administration the patient is asked about glaucoma In general, a history of glaucoma is taken as a contraindication to its use.

We have recently treated a patient with a negative history of glaucoma, who developed acute closed-angle glaucoma within 12 h of a barium meal investigation in which Buscopan 20 mg was given as an intravenous hypotonic drug As a result we suggest that the routine questioning in this situation be modified.

The anticholinergic effects of Buscopan include pupil dilatation and paralysis of accommodation, the former constituting the risk of serious rise of intraocular pressure in those with unduly shallow ocular anterior chambers. The mydriatic effect usually wears off within 3 h, and is much less marked than that due to dilating eye drops used for diagnostic purposes. In people whose eyes do not have narrow anterior chamber angles, which includes most of those with chronic glaucoma, the ocular side-effects of the drug do not pose a significant threat. The prevalence of chronic glaucoma is estimated to be 0.28%. This is about three times as common as acute glaucoma (Hollows & Graham, 1966). The standard treatment for acute glaucoma is a peripheral iridectomy (or laser iridotomy) after which the risk from pupil dilatation is removed. Prophylactic surgery to the fellow eye is also common practice (Low, 1962).

In routine questioning for glaucoma, only those with chronic glaucoma (probably on medical treatment with eye drops) or those with surgically treated acute or chronic glaucoma will give a positive history We feel that to withold Buscopan in these instances may unnecessarily restrict diagnostic capability On the other hand, if the patient is advised before the injection of the very small risk of its causing acute glaucoma, and that if they should experience sudden eye pain or loss of vision within a few hours they should seek early medical advice, then the rare crisis of acute glaucoma may be averted

Yours, etc.,
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(*Received October 1986*)

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Allergic reaction to Buscopan

THE EDITOR—SIR,

We were interested to read the report by Thomas et al (1986) describing what was almost certainly a reaction to Buscopan (hyoscine-N-butylbromide, Boehringer Ingelheim) We have also recently witnessed a potentially fatal reaction.

CASE REPORT

A 66-year-old man was referred by his general practitioner for a barium meal examination, having had symptoms of upper abdominal discomfort for several months He also suffered from mild asthma, for which he had been prescribed inhaled salbutamol, two puffs four times a day, and beclomethasone, two puffs three times a day. He had no history of specific allergic reactions and was a non-smoker. At the beginning of the examination he was given 20 mg Buscopan intravenously along with several Baritop effervescent tablets (Sakai Chemical Industry Co. Ltd) and 100 ml E-Z-HD barium suspension (E-Z-EM Co Inc). A few minutes later he became increasingly short of breath and wheezy. At the time, these symptoms were attributed to the fact that he had omitted to take his medication for that day, and the combination of the physical exertion in moving on the X-ray table and some degree of anxiety had precipitated an asthmatic attack The examination was discontinued and he was referred to the Accident and Emergency Department, where he was treated with nebulised salbutamol. He quickly improved and was allowed home 1 h later

A further appointment was made 3 weeks later and he was urged not to omit his medication and, immediately before the examination, he was asked to inhale two puffs of salbutamol. He was then given 20 mg of intravenous Buscopan but, before he could swallow any barium, he started to complain of increasing shortness of breath This rapidly worsened and the patient became cyanosed and very distressed. Intravenous hydrocortisone and chlorpheniramine were administered and 100% oxygen was supplied via a mask. After only a few minutes there was considerable improvement and he was again transferred to the Accident and Emergency Department. No further treatment was required and, after observation for several hours, he was allowed home.

As Thomas et al (1986) discovered in the literature, allergic reactions to Buscopan are rare. The reaction of our patient would appear to be an immediate sensitivity-type reaction to Buscopan and, as no barium was ingested, this cannot be implicated in the reaction.

We feel that there may be many unrecorded allergic reactions during barium meal examinations and wider enquiry could reveal that the hypotonic double-contrast barium meal is not such a benign examination as is currently considered.

Yours, etc.,
P. Trewheke
N. K. Barrett

The Department of Radiology,
Charing Cross Hospital,
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(Received November 1986)

REFERENCE

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Min-R film for mammography

The Editor—Sir,

I am pleased to respond to the letter from Drs Kirkpatrick and Law in the December issue (Kirkpatrick & Law, 1986) regarding the proposed discontinuation by Kodak Limited of Kodak Min-R film for mammography.

Although a large number of users have opted for our higher-speed films, it is clear that there are still a significant number of users who find that Kodak Min-R film meets more fully their diagnostic requirements.

Because of this, we have decided to cancel the plans for the withdrawal of this film. It will, therefore, be available for mammography while this significant demand exists. Current users of the product have been informed directly.

Yours, etc.,
D. J. Nobbs

Health Sciences Division,
Kodak Limited,
PO Box 66,
Hemel Hempstead,
Herts HP1 1JU

(Received January 1987)

REFERENCE

Kirkpatrick, A. E. & Law, J., 1986. Proposal to withdraw Min R film (letter). *British Journal of Radiology*, *59*, 1242.

(Authors' reply)

The Editor—Sir,

We welcome the decision by Kodak Limited to continue the supply of Min-R film. They had kindly informed us of this decision early in January.

We understand that supplies of Agfa-Gevaert's Medichrome Blue film, identified in our paper as our current first choice, may be less easily available in the future. This will leave Min-R as our first choice until another film is found which gives both better image quality and lower dose.

Yours, etc.,
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J. Law

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1987, *The British Journal of Radiology*, *60*, 419–421 APRIL 1987

Proceedings of The British Institute of Radiology

Endoscopy and its relationship to radiology

Abstracts of papers presented at the above meeting, held jointly by The British Institute of Radiology, The Royal College of Radiologists and The Royal Society of Medicine (Section of Radiology) at 36 Portland Place, London W1N 4AT on Thursday, January 16, 1986

Chairman: Dr J. N. Glanville

Introduction, by J. N. Glanville
Endoscopy in the radiology department: a radiologist's point of view, by A. H. Chapman
Upper digestive tract endoscopy, by R. A Frost
Therapeutic endoscopy in upper gastrointestinal bleeding, by D. E. Beckly
Of polyps and things, by D. F. Sheppard Abstract not received
ERCP and sphincterotomy et cetera, by M I. Lavelle
Angioscopy, by D. C Cumberland
Nasal endoscopy, by J. N Glanville

INTRODUCTION

J. N. Glanville

X-ray Department, St James's University Hospital, Leeds

The British Institute of Radiology has recognised endoscopy as being a full part of a diagnostic imaging department. The meeting was arranged so that as many aspects of endoscopy as possible within the time limits could be introduced, and all the speakers were practising radiologists

ENDOSCOPY IN THE RADIOLOGY DEPARTMENT: A RADIOLOGISTS'S POINT OF VIEW

A. H. Chapman

Department of Radiology, St James's University Hospital, Leeds

The claim that the barium meal is less sensitive and specific than endoscopy has been made in a number of studies in which endoscopy has been used as the end-point. A recent, carefully constructed study has once again come out significantly in favour of endoscopy (Dooley et al, 1984). Such challenges have, in the past, been taken up by radiologists resulting in the change from a single-contrast to a double-contrast technique and, more recently, to the use of a combined double- and single-contrast (biphasic) examination.

The radiologist who is able to endoscope his patients can monitor the barium radiology in his department and, by analysing the mistakes made, can modify and develop his radiological technique. He will realise the importance of paralysis, good coating and the correct amount of distension of the stomach and duodenum, and will become aware of the type of study that leads to mistakes being made. Laufer has pointed out that when he is confident as to the quality of an examination then its accuracy comes close to that of endoscopy (Laufer, 1976). An indication of the radiologist's confidence in the study can, therefore, be a valuable addition to the radiographic report.

Patients seem to find little to choose between radiology and endoscopy (Dooley et al, 1983) and those who find it difficult to turn when on an X-ray table often express a preference for endoscopy. Endoscopy is the investigation of choice for acute upper gastrointestinal bleeding and for elderly, debilitated and unco-operative patients who are difficult to examine radiologically. The complications of endoscopy exceed those of barium radiology, but many are cardio-pulmonary (Silvis et al, 1976) and probably result from its use in severely ill patients where endoscopy offers the only hope of an accurate diagnosis. However, the mortality rate of one in 15000 for upper gastrointestinal investigation militates against its routine use. Radiology still has a role to play as it is a safer and less expensive examination; therefore, its continued use can be justified as the initial investigation of upper gastrointestinal complaints in ambulant patients, where a high-quality examination can be obtained.

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UPPER DIGESTIVE TRACT ENDOSCOPY

R. A. Frost

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The fibreoptic endoscope has established a major role in imaging. Excellent optics and angling capabilities now ensure that no point in the oesophagus, stomach or duodenum is hidden. The initial explosive growth has slowed, but continues at 14% per annum for diagnostic endoscopy Barium protagonists have responded to this challenge by refinement of double contrast techniques and while both procedures can be very accurate, endoscopy more consistently demonstrates fine mucosal detail and has the edge on radiology for accuracy Standards vary and only local audit can determine comparative accuracy in a particular institution There should now be little difference in terms of safety and cost and, contrary to popular belief, more patients prefer endoscopy.

Each investigation has particular strengths. Those of radiology are the demonstration of function, such as oesophageal mobility and gastric emptying, and the production of an anatomical map. Endoscopy allows visualisation of finer mucosal detail and enables biopsy and therapeutic manoeuvres. Barium-meal demonstration of gastro-oesophageal reflux or duodenal ulceration will require no further investigation unless treatment fails. However, in patients over 50 years of age, if early gastric cancer is to be found, there is a strong case for endoscopy in barium-negative dyspepsia. Equivocal barium lesions lead to endoscopy and many gastric abnormalities require biopsy. Should endoscopy, therefore, usually be performed in the first instance? Certainly it is the absolute investigation of choice in acute bleeding, in a previously scarred duodenal cap, in the post-operative stomach, and in elderly, immobile or disabled patients who find the double-contrast meal a great ordeal.

Endoscopy, an imaging procedure, is primarily undertaken by medical gastroenterologists. However an increasing number of radiologists perform endoscopy, and it is logical that they should do so. Close co-operation between endoscopist and radiologist improves the quality of both techniques and enables the correct investigation to be selected, so that unnecessary duplication is avoided. The specialist gastrointestinal radiologist should have an opportunity for endoscopy training in order to play a full role in the gastroenterology team.

THERAPEUTIC ENDOSCOPY IN UPPER GASTROINTESTINAL BLEEDING

D. E. Beckly

Department of Radiology, Plymouth General Hospital, Plymouth

Current techniques being applied to the endoscopic treatment of bleeding peptic ulcers were outlined. Emphasis was placed on the need for accurate prediction of which ulcers are at risk for serious recurrent bleeding. The author's experience with an endoscopic Doppler device was described and it was shown that this enabled a more accurate prediction of recurrent bleeding to be made than was possible using visual appearances alone. Sixty untreated peptic ulcers were studied. "Rebleeding" was defined as recurrent bleeding after the initial bleed of sufficient severity to require surgery for haemostasis or lead to the patient's death from exsanguination. Nine of 16 Doppler-positive ulcers rebled while only three of 44 Doppler-negative ulcers did so. Thirty-one ulcers were treated by Nd YAG laser. In 15 cases active bleeding at the time of endoscopy was stopped by laser coagulation and two of these patients rebled. In eight cases laser coagulation converted a Doppler-positive ulcer to Doppler-negative and two of these patients rebled. In eight cases a Doppler-positive ulcer remained Doppler-positive in spite of laser coagulations and five of these patients rebled. It was concluded that statistically significant improvement in prediction of rebleeding risk in untreated ulcers could be made by the use of Doppler ultrasound. The method also shows promise of being useful in assessing the adequacy of laser coagulation and predicting treatment failures.

ERCP AND SPHINCTEROTOMY ET CETERA

M. I. Lavelle

Department of Radiology, The Royal Victoria Hospital, Newcastle-upon-Tyne

In this section of endoscopy there is close co-operation between radiologist and endoscopist. Endoscopic retrograde cholangiopancreatography (ERCP) is performed in the imaging department as good fluoroscopy and spot films are essential to the procedure. Initially diagnostic and mainly pancreatic, the workload is now largely biliary and therapeutic, to deal with gallstones and, more rarely, strictures or tumours. Endoscopic sphincterotomy (ES) allows removal of common duct stones with a balloon catheter or dissolution by infusion of mono-octonoain through an endoscopically inserted cannula.

Results of 247 cases where ES was performed were presented showing an 88.7% success rate in removing the stones, 12% major complication rate and 2.4% mortality, four of these six cases being myocardial infarction or cerebrovascular accident occurring within a month of the procedure.

In cases of bile-duct carcinoma or stricture, ES allows the insertion of an endoscopic prosthesis and the technique was described, stressing the value of radiological assistance.

Endoscopic retrograde cholangiopancreatography remains of value in the management of chronic pancreatitis, including cases where alimentary blood loss results (Hall et al, 1982) and also pre-operatively in pancreatic trauma to show the site of damage.

Digital subtraction techniques have been combined with ERCP (Lavelle et al, 1985) and appear especially valuable in showing space-occupying lesions of the parenchyma. This joint endoscopic and radiological procedure showed a 1 cm-diameter insulinoma not revealed by angiography or computed tomography.

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ANGIOSCOPY

D. C. Cumberland

Department of Radiology, Northern General Hospital, Sheffield

The last 2 years or so have seen the availability of smaller and more flexible endoscopes, making the long-held hope of direct intravascular visualisation a feasible proposition. For purely viewing purposes, instruments of 5 French diameter are available, and there is one of approximately 7 French diameter with a "working channel" able to carry a 0.020 in guide wire, laser fibre or possibly microsurgical instruments; both can be introduced through a standard arterial sheath. Proximal occluding balloons and vigorous flushing are needed to clear the field of blood, though good quality images can be obtained in the iliac artery, antegrade femoral visualisation is very difficult because of persistent collateral blood flow. Developments in balloon occlusion, either via a guiding catheter or on the instrument itself, are necessary before percutaneous angioscopy becomes diagnostically acceptable or useful.

Possible future uses include the differentiation of lesions shown by arteriography, such as residual thrombus versus underlying stenosis after fibrinolytic therapy or the diagnosis of acute complications after angioplasty, such as thrombosis, spasm or dissection. Laser energy holds promise in assisting percutaneous angioplasty, but perforation due to lack of specificity is a major problem. Angioscopically-guided delivery is one possible means of assuring a luminal route, but in one study there was a significant instance of perforation despite intra-operative visualisation (Abela et al, 1985). Some substances such as haematoporphyrin derivative are preferentially absorbed by atheroma; it is then possible *in vitro* to use a laser of appropriate wavelength to ablate selectively the atheroma

(Vincent et al, 1985). The clinical applicability of this remains to be seen

Intra-operative angioscopy, which allows a relatively bloodless field, is more feasible than percutaneous introduction and it is already showing promise as a means of checking grafts and anastomoses (Van Stiegmann et al, 1985), and dealing with venous valves during *in-situ* grafting. Of more immediate interest and potential use for the radiologist is the application of these fine angioscopes in other body systems, such as the biliary and urinary tracts, the bronchi or even the spinal canal. Avenues may thus be opened for radiologically controlled diagnosis and interventional therapy.

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NASAL ENDOSCOPY

J. N. Glanville

X-ray Department, St James's University Hospital, Leeds

It has been estimated that 4–8% of children of primary school age have speech difficulties, mostly hypernasality. The previous method of investigating the efficiency of the velo-pharyngeal sphincter was by coating it with barium and recording its movements during speech in the submento-vertical, postero-anterior and lateral views. This was compared with the newer method of direct visualisation of the muscle movements as viewed by an endoscope introduced through the nose. Pros and cons of both methods were discussed. Endoscopy had the advantage of being a direct viewing method with no radiation and greater ease in interpreting complex post-operative appearances. Its disadvantages were the inability to take measurements, the need for a high level of local anaesthesia and a troublesome flaring of the image.

The advantages of the radiological method were the ability to view movements in the three positions, the possibility of taking accurate measurements and the absence of need for any preparation. The disadvantages were the use of radiation, a longer procedure time and the need for training in interpreting the recorded images.

Book reviews

Radionuclide Imaging in Medicine Theory and Practice By Peter C. Jackson, pp xi+251, 1986 (Farrand Press, London), £18.00
ISBN 1-85083-003-7

This book describes the physics and technology of radionuclide imaging: some basic radiation physics, the operation and performance of the Anger gamma camera, data-processing hardware, imaging analysis and digital processing A chapter on techniques covers the basis of static and dynamic imaging and cardiac-gated acquisition, and includes a detailed treatment of single photon emission tomography It is intended as a basic text for medical, scientific and technical personnel. Each section subheading is given a "star rating" to indicate whether the content is of elementary, intermediate or advanced level, the reviewer was unconvinced of the value of this unusual and rather distracting device.

The depth of content is somewhat uneven. For example, Compton scattering is described with the inclusion of equations to derive the frequency of scattered photons, but radionuclide decay schemes receive little attention. The production of radionuclides, the principle of generators and the value of isomeric transition are not discussed at all, nor is anything included on radiation dosimetry

The book's strength lies in its detailed treatment of the Anger gamma camera The principles of collimation, scintillation detection and electronic analysis are described with the aid of extremely clear diagrams. Emphasis is placed upon the quantification and assessment of performance (for both projection and tomographic imaging) so that the text may be useful as a primer for those interested in quality control. Unfortunately, the description of gamma camera electronics stops short of the microprocessor-controlled energy and linearity correction circuitry employed in most modern systems. The only method of uniformity correction described is that of regional sensitivity adjustment—now largely discredited.

The style is generally clear but the method of production of the text (directly from disc supplied by the author) seems to have left several misprints and one or two typographical peculiarities. The reproduction of the halftones is not always good and the two colour plates are rather unsatisfactory.

There are a few references at the end of each chapter but they are by no means comprehensive. There are four appendices which could have contained useful information but suffer from lack of accuracy and clarity. A table of conversion factors between CGS and SI units, for example, does not indicate how the conversion factors are to be used, and does not even tabulate the various factors in the same sense.

There is the basis of a useful publication here, which could perhaps have benefited from some constructive independent refereeing and more meticulous attention to detail

R. A SHIELDS

Nuclear Medicine in Urology and Nephrology, 2nd edit. By P H. O'Reilly, R. A. Shields and H. J Testa, pp xiii+291, 1986 (Butterworth Group, Sevenoaks, Kent), £53.00.
ISBN 0-407-00322-3

Isotope techniques are widely employed in the evaluation of diseases of the kidney and urinary tract; a comprehensive text expounding their role in a clinical context is a valuable contribution to the diagnostic literature. The first edition of this book achieved classic status and this is enhanced by the improved and expanded new edition The authors have produced a well ordered, compact text covering all of the clinical and many of the research applications of isotopes in this field. It is set out in such a way as to be useful as a reference work as well as forming an eminently readable overview of the subject. This is achieved by dividing off the physics, mathematical and technical aspects into a separate section, intended for reference. This discussion of clinical applications and their evaluation in the context of other techniques thus occupies the first part of the book and it is to this that physicians concerned with the renal tract and those whose interest is in imaging will turn first of all.

They will find here a comprehensive and carefully argued exposition of the applications of isotopes with their limitations and interrelations with other available techniques Renography, perhaps the most useful application because of the functional information it provides, is covered in detail but at a practical level, stressing those analytical procedures that are of proven value and are readily available, rather than the more esoteric deconvolution methods. Imaging techniques using isotopes are, properly, given less emphasis. Subsequent problem-orientated chapters evaluate the role of these methods and the role of clearance studies for measuring glomerular filtration rate in obstructive uropathy, renal mass lesions, trauma and renal transplants. Paediatric applications receive separate treatment, as do specific nephrology problems such as the investigation of hypertension

This is an excellently produced textbook with clear illustrations that are well chosen and captioned. Physicists and nuclear medicine specialists will need a reference copy and it is strongly recommended to all clinicians involved in the fields of nephrology and urology

D. O. COSGROVE

1986 Nycomed Scholarship Reports

Dr Anne Hemingway and Dr Amman Bolia, the winners of the 1986 Nycomed Scholarships, spent September and October in radiology departments in Scandinavia. This month's *Bulletin* features their reports.

ANNE HEMINGWAY

I was based for the entire eight weeks of the Scholarship in the University Hospital, Lund, Sweden I was attached to the gastroenterology section of the Department of Radiology under the direction of Professor Anders Lunderquist There were three major aspects to my visit: clinical, research and social. I will discuss each area separately. While based in Lund I had the privilege of visiting the department in Malmo on two occasions and was invited by Professor Torsten Almein to deliver a guest lecture I also delivered two lectures to the department in Lund.

Clinical

The University Hospital of Lund is situated on the outskirts of the city centre. It is a relatively new complex and has between 1500 and 1800 inpatients The Department of Radiology is situated on three floors in the central block On the first floor one finds the units of paediatric, orthopaedic and neuroradiology. The latter unit has a computed tomography (CT) scanner and has just installed a magnetic resonance scanner and a digital vascular imaging system

On the second floor are the filing area, secretariat, doctors' offices, library, and reporting and conference rooms. It is the policy of the department (and many others in Sweden) that no radiograph ever leaves the department There are numerous daily clinical conferences and clinicians come to the department to see films All radiographs are reported almost immediately by an experienced radiologist The third floor of the department comprises urology, gastroenterology, CT, ultrasound and angiography.

The radiologists are system rather than modality orientated Professor Lunderquist's team are responsible for all gastroenterological and hepatobiliary procedures including barium examinations, interventional procedures, angiography and abdominal CT The quality of barium work was particularly impressive

The role of the technicians (radiographers) in the department is somewhat greater than in England For example, they perform most of the nursing duties, put down nasogastric tubes, and can administer intravenous drugs, including contrast medium for intravenous urograms, CT scans etc The working day starts between 7 a.m. and 7.30 a.m. and finishes at 6 p.m The majority of clinical work is completed by 4 30 p.m. when the auxiliary and paramedical staff go home, except for those on emergency duty In comparison with my own department they are very well staffed, having a total of 45 radiologists (35 qualified and 10 in training).

I was able to observe a wide variety of investigations and took a particular interest in angiography There were a number of differences of technique which provided valuable additional experience

Research

The most valuable experience that I gained while in Lund was the chance to learn research techniques and to become involved in some ongoing research programmes. The University has extensive facilities for research. I was involved in three separate projects during my visit The first was to assess the effect of balloon dilatation of the duodenal papilla as an alternative to sphincterotomy. This project will hopefully be completed in late December and we hope to publish the results in the New Year.

The second project involved learning operative techniques for cannulating the duodenal artery and vein in order to study the effects of embolisation of liver tumours using an oil emulsion mixed with cytotoxic agents Much basic work in this subject has been carried out in Sweden and Japan and initial laboratory and clinical results are very encouraging. I anticipate setting up a similar model in Britain to continue the work.

The third project was concerned with vital microscopy techniques. Liver tissue can be examined *in-vivo* under very high-power microscope techniques, allowing direct visualisation of hepatocytes, sinusoids and Kuppfer cell function This fascinating technique allows direct assessment of uptake of oily contrast media, and *in-vivo* assessment of tumour behaviour and embolisation techniques The possibility of setting up a similar project in my own institution is being investigated

Social

Lund is a university town in southern Sweden. The town itself is quite small, everything being within easy walking distance. The most popular means of transport is the bicycle Within the town centre, is a number of fascinating museums and historical churches. The cathedral is very old and boasts a beautiful astronomical clock. There were regular organ recitals one evening a week and on Saturdays. While I was in Lund I was fortunate to be able to attend a performance of *Ghengis Khan* by "Lundaspex" This satirical play was staged by an entirely male cast drawn from the University and was performed in faultless English. It was an immensely funny performance and was attended by the King of Sweden. It was one of the most memorable social events in the visit.

Lund is very conveniently situated for visiting a large number of other towns and cities in the vicinity Malmo (the third largest city in Sweden) is a 15-minute train journey from Lund From there I was able to cross very easily to Copenhagen. I visited Copenhagen twice, the first occasion (in the pouring rain) was devoted to two of the city's museums, although despite the rain I did also see the Little Mermaid. On the second occasion I visited the Cook factory and spent a fascinating day watching catheter, guidewire, coil and filter production.

Just a little further north from Lund lies Helsingborg and after a 20-minute ferryride one is in Helsingør (Denmark) and can visit Elsinore (Hamlet's castle). I also managed to spend a day and a half in Stockholm; this was not nearly enough time to do this beautiful city justice In that short time I was able to get only a very rapid and superficial impression of the city and unfortunately as winter and October had arrived a number of the museums were closed

Conclusion

The Nycomed Scholarship provided me with an excellent opportunity to visit, and become involved in the work of, another department I was able to consolidate friendships already established with Swedish radiologists and I hope these will provide valuable links between our departments for many years to come I have no doubt that future recipients of the Scholarship will also benefit enormously from their studies in Scandinavia

I would like to express my thanks to Nycomed for their generosity in funding this scheme, the BIR Committee for organising it and Professor Anders Lunderquist, Professor Eric Boijsen and all the staff in Lund for making my visit so worthwhile and enjoyable

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AMMAN BOLIA

Uppsala

My first week of the Scholarship was spent in the Ultrasound Department of the University of Uppsala in order to learn ultrasound-guided biopsy techniques. The academic hospital is a huge complex with over 1500 beds, typical of one of the seven or so Akademiska Sjukhusets in Sweden. The hospital caters for about 250 000 inhabitants in and around Uppsala, but also acts as a referral centre for approximately one and a half million people. All the major specialties are represented at this centre.

Dr P. G. Lindgren is in charge of the Ultrasound Department and, with Dr T. Anderson, examines some 5000 patients per year Dr Lindgren has devised a biopsy gun that enables the use of a Tru-cut needle with one hand, so leaving the other hand free to hold the ultrasound probe. The gun basically consists of a spring trigger system for firing the two parts of a Tru-cut needle. The needle is introduced under ultrasound guidance; the tip is easily visualised and is brought to just within the lesion and the trigger is fired. The needle moves by at least 2 cm, so the tip has to be at least this distance away from any vital structure. Usually only one pass is necessary, as good specimens are almost always achieved An 18G needle is used Almost any mass lesion in the abdomen, detected by ultrasound, can be biopsied with this needle with no serious complications. With a 14G needle, however, in 32 splenic biopsies, four patients needed transfusion and one required splenectomy

On an average day approximately 20 ultrasound examinations were carried out, including two or three biopsies. One or two of these might be renal transplant cases Some of the biopsy cases were formally requested by clinicians but generally, if the lesion seemed suitable, it was at the discretion of the radiologist. Interestingly, there was not the formality of a form of consent

Copenhagen

I spent two days at Herlev, a modern hospital in the suburbs, to see a different aspect of interventional ultrasound. There were various important differences compared with Uppsala. Dr Holm, a urologist, is in charge of the Ultrasound Department, which he said worked completely independently of the X-ray Department

There were at least four ultrasound machines. The medical staff were mainly urologists but at least one was a radiologist, who was not then attached to the Radiology Department. Technicians could report ultrasound examinations, but interventional procedures, for example ultrasound-guided abscess drainage, percutaneous nephrostomy and biopsies, were carried out by the medical staff.

Each day approximately 25 examinations were carried out, of which two might require some form of intervention. The practice of percutaneous ultrasound-guided biopsy was quite different to that in Uppsala. A fine needle (21–23G) was used, with three passes for aspiration cytology biopsy and a further three passes using a 21G Surecut needle to obtain a core specimen. (It was difficult to be convinced that good core specimens, adequate for histological examination, could be achieved using such fine needles but apparently they were sufficient for diagnosis) A lumbar puncture type of needle was used as a supportive guide through the abdominal wall so that a fine needle could be introduced through it.

The Ultrasound Department at Herlev works in close collaboration with the Danish firm Bruel and Kjaer, which manufactures ultrasound machines. One of the interesting developments has been an intravaginal probe which gives good visualisation of the uterus and ovaries and, unlike the suprapubic examination, does not need an overfull bladder This transvaginal method of ultrasound guidance is adopted, as a matter of choice, for aspiration of ova for *in-vitro* fertilisation in Gothenberg, Sweden

During my stay in Copenhagen, I learnt about several other interventional ultrasound-guided procedures, including the treatment of parathyroid adenoma with absolute alcohol, the treatment of prostatic carcinoma with Iodine-125 seeds, catheterisation of the pancreatic duct, transhepatic splenoportography and venous sampling of hormone-secreting tumours of the pancreas.

Dr Holm has a superb collection of video tapes of various procedures and interesting cases, which I was privileged to view during my free time

Lund

Four weeks (except two days in Copenhagen and one day in Malmo) were spent at Lund in the X-ray

Department, under Professor E. Boijsen. There the working day for most staff is 8 a.m to 4 p.m, but many radiologists start much earlier. As in most Scandinavian institutions, the day's work starts with a clinico-radiological conference. Some 50 or so of the surgical team, including students and trainees of various grades, attend the meeting The meetings, of course, are normally in Swedish, but we were greatly honoured when the meetings were conducted in English just for the benefit of two British radiologists. Some 20 or so examinations, done the previous day, are presented The radiologist is very much in charge of the meeting. He appears to do most of the work, reading out the patient's clinical details and showing the radiographs, while the clinicians sit, watch and listen

Such meetings are essential, as no radiograph leaves the X-ray Department except when needed in theatre. One of the great advantages of such a system is that previous radiographs are almost always available at the time of reporting, and before the start of any procedure, *i.e* retrieval of radiographs is almost 100%, unlike in the UK where films may be on the ward, in the outpatients or X-ray department, with medical secretaries, in a consultant's office, or with a porter/nurse somewhere between these departments.

The reporting is usually "hot" for inpatient procedures and plain radiographs The request card is hardly a card as we know it, but an A4 sheet Clinical detail on such a form is usually comprehensive No patient signs a consent form for radiological procedures, including interventional procedures but an enormous amount of detail is documented by the radiographer/radiologist. For a femoral arteriogram for example, the type of needle and puncture site, size, shape and type of catheter(s) used, type and amount of contrast medium, number of injections and the rate of injection at each stage, time taken over the procedure, and details of any reactions to contrast medium, etc., would all be recorded

I saw only one biliary drainage procedure and one repositioning of the drainage catheter during my four weeks in Lund This probably reflects the general trend towards endoscopic biliary procedures, which have fewer complications

Percutaneous nephrolithotomies /nephrostomies averaged about one to two per week In the case of percutaneous nephrolithotomy, the radiological half of the procedure (creating a channel to the pelvicalyceal system) was done in the X-ray Department, while the other half took place in the urology theatre. Ultrasound guidance occasionally proved a useful way of getting into the pelvicalyceal system, either for percutaneous nephrostomy or nephrolithotomy

Vascular Intervention was limited in terms of numbers, except for percutaneous transluminal coronary angioplasties which numbered two to three per week There was one splenic embolisation, four percutaneous transluminal angioplasties and one percutaneous transluminal renal angioplasty during my stay. A simple straight catheter was widely used for angiography. This same catheter could then be shaped as required with a copper wire placed in the tip and using near-boiling water followed by rapid cooling in cold water Side holes are also made as required just before the procedure.

Coeliac ganglion block procedures averaged one or two per week and were previously done by the anaesthetists "blindly" Nowadays, they are carried out entirely by radiologists in the X-ray Department under screening control. A catheter with a simple curve (sidewinder type 1) is placed in the coeliac trunk. The patient is then turned prone and a fine needle is introduced in the postero-lateral plane. Using a screening in two planes, the needle is positioned just anterior to the tip of the catheter where one expects the coeliac ganglion to be The injection of a small amount of contrast medium is used to confirm the position and to ensure that the artery is not punctured. Then 15 ml of a mixture of absolute alcohol and local anaesthetic is instilled. Good results have been achieved in patients with intractable pancreatic pain. The procedure is repeatable when the pain recurs No complications have been encountered so far in Lund.

Malmo

Dr Anne Hemingway and I paid a one-day visit to Dr Almen's department in Malmo, some 20 km from Lund This giant of a hospital, with 1700 beds, is no less impressive than the other Akademiska Sjukhusets in Sweden. Some 250 000 examinations a year are done in the X-ray Department in Malmo This includes 5200 CT scans per year on one CT scanner, 2200 venograms per year and 50 to 60 mammograms per day! A magnetic resonance scanner had recently been installed

In the archives, all the radiographs done since 1898 have been collected (over 88 years of radiographs!—Placed end to end they would stretch 75 km!) The radiographs are filed under "part of the body examined" and "pathology"

Oslo

There are three major teaching hospitals in Oslo, Ulleval Hospital (1500 beds), Rikshospitalet (National Hospital) and Aker Sykehus (800 beds) My attachment for three weeks was at Professor Ivar Enge's X-ray Department at the Aker Sykehus. The working day starts at 7.00 a.m and finishes at 3.00 p.m As in Sweden, the day starts with a clinico-radiological meeting and all the films remain in the department.

In the field of interventional radiology, the radiologists, like Professor Enge, were all active. This was particularly so in uroradiology. The cases were quite challenging, particularly the large staghorn calculi the two cases I saw were typical triphosphate-type. In each case 90% of the stone was removed percutaneously, with the help of the ultrasonic fragmenter. The remainder was dealt with by the shock-wave lithotripter at the Ulleval Hospital

All three hospitals in Oslo have acquired the new Trimedyne laser equipment for use in peripheral vessel disease. Within the first week of my arrival, the first patient underwent laser treatment with success. During my stay, two further patients were also treated.

An interesting afternoon was spent with Mr Renes, the Manager of the Medical Department at Nycomed International in Oslo. The organisation has a very well equipped library, with access to medical literature on computer, as well as conference rooms and well equipped research laboratories.

Training in radiology

After five and a half years of medical training, a doctor has to spend a further two years of internship before being able to practise. To become a radiologist requires a further four and a half years in a recognised radiology training centre. In Sweden, as in Norway, there are no higher qualifying examinations. The only requisite for a trainee radiologist is to attend six one-week courses during the training period During my stay in Lund, there was such a one-week course, in gastrointestinal radiology, for trainees.

Research

Research plays a prominent part of the radiologist's career, whether one is a trainee, fully qualified, or a professor in the radiology department. Specific time is devoted by most staff to research, in very well equipped and purpose-built facilities which also cater for animal work. In Uppsala, Friday afternoon was devoted to research for all staff. In Lund people suit their own time for work in their research laboratories.

Summary

I spent eight weeks visiting various departments in Sweden, Denmark and Norway, and witnessed the high standard of radiological practice for which Scandinavian radiologists are renowned. In the field of interventional radiology, a number of hospitals are attempting many different procedures. For a visitor to Scandinavia, it is not easy to achieve an indepth experience in any one aspect of interventional radiology, but one can achieve a broad overview of numerous techniques. In this respect, it has been a worthwhile experience, thoroughly recommended to any intending visitor.

I would like to thank the heads of departments mentioned above for having me in their department, and all the Scandinavian radiological colleagues for their friendliness and willingness to teach. Last, but not least, I would like to thank Nycomed for providing generous funding, The British Institute of Radiology for organising the Scholarship, which made this venture possible, and the people at Nycomed (Oslo) for being such good hosts.

BIR Welsh Branch: 1986 Autumn Meeting

The Autumn Meeting of the Welsh Branch of the BIR was held at the University Hospital of Wales, Cardiff, on Saturday, November 8, 1986 An informal reception incorporating a trade exhibition organised by 3M Ltd and J Otley Rhodes Ltd was held on the Friday evening. The scientific meeting was chaired by Dr Rosemary Anderson. Abstracts of the lectures are given below

The 1987 Spring Meeting, to be organised by Dr Hywel Davies, will be held in Aberystwyth.

Radiology of the salivary glands

Dr A Whyte

Congenital disorders of the salivary glands include agenesis, atresia and aberrancy. Agenesis leads to diminished saliva production and may be demonstrated to be partial or total by computed tomography (CT) or $^{99}\text{Tc}^{m}$ pertechnetate studies. The commonest aberrant site for salivary-gland tissue is in Stafne's bone cyst in the mandibular angle. Calculi and their sequelae of chronic sialadenitis should be investigated by a combination of plain radiographs and sialography Up to 40% of parotid calculi are radiolucent Chronic sialadenitis leads to characteristic pruning of peripheral ducts and alternate narrowing and dilatation of the main duct Autoimmune disorders include several conditions which, however, produce identical sialographic changes of sialectasis and diffuse dilatation of the main duct. A radiological technique used for evaluating salivary-gland mass lesions should ideally distinguish intraglandular from extraglandular lesions, locate the lesion within the superficial or deep lobes and predict whether a lesion is likely to be benign or malignant. Sialography fails on all counts.

Ultrasound (US) and CT were compared in the evaluation of parotid mass lesions, over a one-year period, 20 patients were examined by CT, US or both. The position of the facial nerve can be estimated by both Benign tumours appear well demarcated by both techniques, have a homogeneous echo pattern on US and are denser than normal gland on CT. Malignant tumours have poorly demarcated boundaries and inhomogeneous echo and density patterns and CT may demonstrate spread outside the gland. Ultrasound should be used for the initial assessment of mass lesions and for localising abscesses in patients with acute parotitis If US shows tumour spread medial to the mandible, incompletely visualised boundaries or spread outside the gland, CT with intravenous contrast medium should be performed.

Radiology of the sacroiliac joints

Dr J. V Byrne

The joint space of the sacroiliac articulation is oblique in both axial and coronal planes. The obliquity reverses between the ventral and dorsal parts of the joint in the coronal plane. This configuration restricts conventional radiographic demonstration of the joint margins. However, plain radiography remains the primary radiological technique in the demonstration of inflammatory sacro-iliitis. The role of gallium and polyphosphate bone scanning in this situation was compared with the important contribution they can make in the early diagnosis of infective sacro-iliitis. Sclerotic bone reactions around radiologically normal joint spaces in 12 patients were presented. Bilateral sclerosis confined to the iliac margins was seen in six patients (four female), both sides of the joints (one female), both sides associated with marginal osteophytosis (two male) and unilateral sclerosis in association with shortening of the contralateral lower limb (one female and two male). The role of stress and other factors in the aetiology of these signs was discussed.

Radiology of the orbits

Dr R. J. Etherington

The globe of the eye is unique in its accessibility to non-invasive investigation by an ophthalmoscope. Before the advent of high-resolution CT, assessment of the rest of the orbit often necessitated invasive investigative techniques. Plain radiography and CT are now the primary modes of investigation of orbital disease. Several examples of congenital, infective, vascular and neoplastic disease causing plain-radiograph abnormalities were presented, with confirmation of their presence and extent using CT. The usefulness of CT in the assessment and differential diagnosis of retinoblastoma was shown, with reference to its ability to detect calcification within the tumour Computed tomography is also useful when plain radiography is negative, especially in the investigation of proptosis. Examples of the CT diagnosis of dysthyroid exophthalmos, orbital inflammatory pseudotumour and haematogenous metastatic disease were shown The presence and site of intraorbital foreign bodies can be determined by CT and ultrasound. An example of localisation by CT was shown in a case where limbal ring films and ultrasound had been inaccurate. Orbital fractures were described with emphasis on the importance of early recognition of these serious injuries

Radiology of stridor in children

Dr R. Clements

The neck radiographs of children with stridor examined in the Radiology Department of the University Hospital of Wales between 1981 and 1985 were reviewed. Examples of epiglottitis, retropharyngeal abscesses, foreign-body aspiration, laryngeal papillomatosis, subglottic haemangiomas and congenital vascular anomalies were presented.

Radiology of the parathyroids

Dr M. J. Hayward

The first recorded description of hyperparathyroidism was by Thomas Cadwallader, the son of a Welsh Quaker who emigrated to North America. His description predates that of Von Recklinghausen's by 140 years. The first pathological specimen was reported by Sir Richard Owen, the curator of the Hunterian Museum in 1862. The early role of pneumomediastinography, barium studies and angiography were discussed. The advent of newer, non-invasive techniques have improved the localisation of parathyroid lesions. However, there are considerable problems with both CT and ultrasound in a previously explored neck because of loss of normal fascial planes, and CT is also very limited in the mediastinum. Nuclear medicine potentially offers a great advantage over CT and ultrasound, particularly in the explored neck. However, many results do not live up to the early promise and our own results have an overall accuracy of only 70%. Venous sampling probably remains the investigation of choice in difficult cases.

Unusual lung tumours

Dr M. Crane

A series of unrelated cases was presented. The first four cases were of solitary lung masses which all showed marked enhancement on CT after administration of contrast agent. A pulmonary artery aneurysm was considered possible but the lesions proved to be a pneumocytoma (haemangioma), a typical carcinoid, an adenocarcinoma and oat-cell carcinoma: enhancement does not equate with aneurysm. A patient with bilateral chest lesions and liver abnormalities thought to be metastases proved to have a pleural fibroma, a diaphragmatic hernia and benign liver cysts. Tissue diagnosis and CT densities gave the correct diagnosis. A case of endocarditis causing cerebral infarcts in a patient with lung cancer was also presented. Clinically the patient was thought to have cerebral metastases. Cases of both rounded atelectasis and primary pulmonary lymphoma mimicking lung cancer were presented and their radiographic features reviewed. The last patient discussed developed bilateral pulmonary shadowing some years after renal transplantation and an anal carcinoma. The diagnosis was neither metastatic disease nor infection but non-Hodgkin's lymphoma associated with the use of immunosuppressors. This relationship was reviewed.

BIR Awards 1987

The Röntgen Prize

The Röntgen Prize is awarded to Professor W. Duncan, F.R.C.R., F.C.R.P.E., F.R.C.S.E., and the team at the Western General Hospital, Edinburgh, for their many distinguished publications in the field of radiotherapy, especially their studies of neutrons in radiotherapy.

The Barclay Medal

The Barclay Medal is awarded to Dr J. L. Haybittle, M.A., Ph.D., for his contributions to the Journal over more than 30 years on the physical techniques and dosimetry of electron and photon therapy and on the design and statistical analysis of clinical trials in radiotherapy.

The Barclay Prize

The Barclay Prize is awarded to Dr Janet Husband, M.R.C.P., F.R.C.R., for her many contributions to the Journal on the use of computed tomography and other techniques, particularly in the investigation and management of malignant disease.

The awards will be presented at the Conversazione on May 20 at the Royal Naval College, Greenwich.

The BIR Nycomed Scandinavian Scholarships 1988

The British Institute of Radiology invites applications for the 1988 Nycomed Scandinavian Scholarships. These Scholarships, which are generously funded by Nycomed (UK) Ltd, enable United Kingdom diagnostic radiologists, preferably members of the British Institute of Radiology, to visit Scandinavian academic departments for up to two months' concentrated study, free of financial constraints (a maximum of £2500 per month will be provided).

A condition of each scholarship is that a report be submitted for publication in the Bulletin of the British Institute of Radiology.

Applications should be submitted by July 31, 1987, and interviews will take place in September.

For further information please write to: The General Secretary, The British Institute of Radiology, 36 Portland Place, London W1N 4AT.

Electromedical equipment for Europe

British Standards Institution Testing Services recently organised a seminar under the chairmanship of Mr Michael Williams, Director General of the British Health Care Export Council, on the safety requirements for electromedical equipment in European countries. The seminar reviewed the widely divergent technical requirements between European countries and considered the problems manufacturers might encounter.

British Standards Institution Electromedical Laboratories has established agreements with German and Italian testing authorities enabling UK manufacturers to save considerable time and money in obtaining certification of their products for their customers. However, in spite of EEC Directive 84/539 on electromedical equipment there is still a proliferation of national requirements. Dr D. Potter, the DHSS representative, outlined their procurement objective and explained the DHSS role in establishing standards and in drafting new EEC directives to give greater clarity to European requirements. The EEC Directive 85/347 on product liability would be adopted in the UK by July 1988. Under this, patients injured by defective products could bring an action against the manufacturer. Speakers from Italy and Germany then described the situation in their respective countries While the UK did not demand mandatory type-testing, the Italian government had issued Decree 128/86 which enabled such testing to be introduced as required. In addition, the Italian testing authority's certification scheme applied to market-place requirements demanded by equipment purchasers The application of Germany's Electromedical Equipment Law, the MedGV, to transitional certification of equipment already in production or use, was described, as was the application of the GS Safety Mark. Generally, the seminar enabled intending exporters to discuss problems, both formally and informally, with a distinguished panel of overseas speakers Forty per cent of the British Health Care Export Council's business is with Europe and six of its top 10 markets are in the EEC

The Protekton Trust

The Protekton Trust was established in 1984 by Brian Mansfield, a medical X-ray engineer, and the Rev Ronald Eske, Pastor of Summer Road Chapel The trust was established in order to make medical equipment, materials and know how available to countries overseas

The Trust aims to contact hospitals and health authorities in order to obtain equipment and materials which are surplus to the needs of the Health Service It will undertake to repair and recondition donated equipment, and to install and maintain it in the countries to which it has been donated. Some of the available units are inappropriate for use in Third World countries, since their complexity makes them difficult to operate and maintain. Countries like Poland and Romania are also short of equipment, but have a well developed infrastructure and no shortage of highly trained technical personnel, and so equipment is also sent to Eastern Europe

The terms of the Trust require that a local church be appointed to act as its agent in the host country, to ensure that the materials and equipment are fully utilised for the benefit of the people. Also, a register is being compiled of engineers and technicians who are prepared to donate their time on a voluntary basis, both in this country and abroad

For further details please contact B.A Mansfield, The Protekton Trust, 176 Herbert Rd, London SE18 3QE.

Press releases

Varian announces two new dual-energy radiotherapy treatment systems

Varian Associates has introduced two new dual-energy radiotherapy treatment systems, the Clinac 2100C and the Clinac 2500C, which combine the Varian switched-guide accelerator with a new concept in microprocessor-based control systems, and new beam-defining and treatment-couch systems. The two accelerators each feature two widely separate X-ray energies with stable high dose rates and a full range of electron beams, providing a truly cost-effective, clinically versatile treatment system.

The Clinac 2100C has X-ray energies from 6 MV to 18 MV and electron beams from 4 MeV to 20 MeV. The Clinac 2500C has X-ray energies of 6 MV and 24 MV and electron beams from 6 MeV to 22 MeV The microprocessor-based control system of these Clinacs expedites all phases of patient set-up and machine control, including special treatment procedures, service and quality assurance procedures The system uses standard hardware and features an open-ended modular design, ready to accommodate future clinical treatment protocols. Redundant safety interlocks, that provide an additional margin of safety, are an important part of the system design The new Clinac treatment couch design permits fast, precise patient positioning for the widest range of clinical treatment fields The couch, which features an extended vertical travel range, allows both convenient patient loading and very large posterior treatment fields.

Further information is available from Varian Associates, Inc, 611 Hansen Way, Palo Alto, California 94025, USA.

Interactive medical videodisc

The Meddix Data videodisc is a comprehensive, structured and highly transportable source of 30 000 medical illustrations for medical and paramedical instruction. An extensive collection of medical illustrations covering a broad spectrum of disciplines is now available on a videodisc player

The Meddix Data videodisc is interactive the user can define the sequence in which the pictures are shown. Combinations of pictures for selected topics can be assembled within minutes using the specially compiled index supplied with the videodisc This flexibility, combined with the unrivalled quality of the pictures, makes this versatile medium the most suitable for implementations in this field

The 30 000 illustrations are high-quality pictures such as radiographs, high-resolution electron and light microscope photographs, graphs and drawings These pictures include typical examples of pathological symptoms, abnormalities, anatomy, surgical procedures and instruments. Classic cases are illustrated by suitable examples, whilst rare or unusual cases appear only if they contribute to the general background and serve to elucidate specific aspects of the classic case.

The user searches for illustrations simply by using the keywords from the main Meddix Data index. Codes distinguish the various categories such as symptoms, organisms, operations, instruments, prostheses, etc., with appropriate subdivisions per category Furthermore, the pictures are categorised according to the technique with which they were made

Further details are available from VNU New Media Group, Dept Meddix Data, De Boelelaan 7, 1083 HJ Amsterdam, The Netherlands

Multitasking machine helps district general hospital meet NHS requirements

A powerful multitasking, multi-user microcomputer from Alpha Microsystems is providing instant on-line access to all radiographic records and reports at the Countess of Chester Hospital. The radiology department previously used a manual record-keeping system, but with 80 000 records and reports a year, automation was the only logical answer.

The hospital's hardware consists of a one-megabyte Alpha Micro AM-1092M with a 400-megabytes Winchester disc, nine terminals and four printers

Radiologists, radiographers and clerical staff make full use of the system, which handles everything from statistics to patients' appointments The total cost so far of hardware and software is £115 000.

Further information is available from Mike Osler, Alpha Microsystems (GB) Ltd, Berkshire House, 56 Herschel Street, Slough, Berks SL1 1PY (Tel 0753-821922)

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated Attendance is open to non-members.

Annual General Meeting
May 14, 1987 at 4 30 p.m

Imaging in Radiotherapy
May 15, 1987
Chairmen Dr D. Thwaites and another to be announced.
Topics are expected to include integrated treatment planning, special imaging techniques, radiotherapy portal imaging, three-dimensional imaging and simulator CT
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM

Conversazione
May 20, 1987
Royal Naval College, Greenwich

Members' use of the Toshiba Room

Members may borrow the Toshiba Room free of charge, subject to availability This conference meeting room seats 16 people with comfort

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1947 Vol. 20 June, October
1954 Vol. 27 January
1955 Vol 28 May, June, July
1956 Vol 29 September
1957 Vol. 30 January, May, July, September, October, November
1958 Vol. 31 All numbers
1959 Vol 32 All numbers
1960 Vol. 33 All numbers
1961 Vol. 34 July
1962 Vol 35 September

Contact Professor H. Miller, 20 Blackbrook Road, Lodge Moor, Sheffield S10 4LP.

British Institute of Radiology 45th Annual Congress, incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting

RADIOLOGY '87

University of Southampton
April 1-3, 1987

The Congress will cover all aspects of radiology—X-ray diagnosis, radiotherapy, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines and includes:
The BIR Mackenzie Davidson Memorial Lecture, by Professor M J Peckham, "The clinical biology of testicular germ cell tumours"
The BIR Mayneord Lecture (sponsored by 3M UK plc), by Miss Frances Fry, "Chernobyl reactor accident—the impact on the United Kingdom"
The RCR George Simon Lecture, by Sir John Batten, "Radiology and cystic fibrosis"
The BIR Presidential Address, by Professor R. J Berry, "The Institute at 90—a time for reappraisal?"

The BIR Annual Dinner will be held at the Polygon Hotel, Southampton, on April 2.

For further information and registration forms please apply to the Assistant Secretary. Programme, The British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel 01-580 4085).

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a m.–5 p m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan

Recent additions to the Library

Alderson, A R. (Ed). Dosimetry and clinical uses of afterloading systems (IPSM Report No. 45) 1986
Fry, F. A. Assessment of intakes of radionuclides: a summary of investigations 1981–1985 (NRPB) 1986
Grech, P , Martin, T. J., Barrington, N. A & Ell, P J.: Diagnosis of metabolic bone disease 1985
Hall, C M. & Lingam, S : Diagnostic paediatric imaging, a case study teaching manual. 1986
Holm, T., Palmer, P. E. S. & Lehtinen, E.. Manual of radiographic technique. (WHO) 1986
Lloyd, D. C , et al: Doses in radiation accidents investigated by chromosome aberration analysis. (NRPB) 1986
Sanders, R. C. & Hill, M. C. (Eds): Ultrasound annual. 1986
Steiner, R. E & Sherwood, T. (Eds). Recent advances in radiology and medical imaging. No. 8 1986

Scientific document

British Standards Institution· *Determination of Image Distortion of Electro-optical X-ray Image Intensifiers.* BS 6801: 1986; IEC 858· 1986.
This document is now filed in the Library.

Graves Medical 1987–88 Catalogue

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3rd European Symposium on Radiopharmacy and Radiopharmaceuticals
May 1–4, 1987
Elsinore, Denmark
Further details: Elisabeth Nørbygaard, The Isotope Pharmacy, 378 Frederikssundsvej, DK-2700 Brønshøj, Denmark.

Blood Vessel Imaging Using Ultrasound Techniques
May 11–13, 1987
Dolphin Hotel, Southampton
Further details: Mr K. N. Humphries, 5 Mossleigh Avenue, Rownhams, Southampton SO1 8FU.

Conference on Health Effects of Low Dose Ionising Radiation—Recent Advances and Their Implications
May 11–14, 1987
Royal Institute of British Architects, London
Further details. The Secretariat, British Nuclear Energy Society at the Institution of Civil Engineers, 1–7 Great George Street, London SW1P 3AA (Tel. 01-630 0726)

5th International Nijmegen Vascular Symposium: angioplasty, vascular surgery, combined approach
May 15–16, 1987
Nijmegen, The Netherlands
Further details· Dr S. H Skotnicki, University Hospital St Radboud, 6500 HB Nijmegen, The Netherlands.

Advanced Seminar on Diagnostic Radiology Dosimetry
May 18–22, 1987
Ispra, Italy
Further details: Carlo Maccia, CEPN, BP No. 48, F 92260 Fontenay-aux-Roses, France (Tel. 1-46 54 76 59).

Current Skeletal Radiology
May 22–23, 1987
Granby Hotel, Harrogate, Yorkshire
Further details: Mr B. F Moran, Postgraduate, Deans Office, Level 7, Worsley Medical and Dental Building, The University, Leeds LS2 9JT

Cardiovascular and Interventional Radiology and New Imaging Modalities
May 25–29, 1987
Sardinia, Italy
Joint meeting of the European and American Societies of Cardiovascular and Interventional Radiology with participation of the Japanese Society.

Further details· Prof. P. Rossi, Instituto di Radiologia della Universita, Policlinico Umberto 1, I-00161, Italy (Tel. 01039-6495 5602).

VI Congress of the European Association of Radiology (ECR '87)
May 31–June 6, 1987
Lisbon, Portugal
Further details· Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123–7° DTo, 1000 Lisboa, Portugal, (Tel: 77–05 30, Telex 62074 SPRMN P).

Euroson '87: 6th Congress of the European Federation of Societies for Ultrasound in Medicine and Biology
June 14–18, 1987
Finlandia Hall, Helsinki, Finland
Further details. Congress Bureau, PO Box 824, SF-00101 Helsinki, Finland

College of Radiographers' Annual Conference
July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel. 01-935 5726, ext. 206).

International Symposium on Dosimetry in Radiotherapy
August 31–September 4, 1987
Vienna, Austria
Further details· Secretariat IAEA-SM-298, c/o International Atomic Energy Agency, PO Box 100, A-1400 Vienna, Austria (Telex No 1-12645. Cable address INATOM VIENNA)

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Further details Dr G. M Steiner, Sheffield Children's Hospital, Western Bank, Sheffield S10 2TH (Tel. 0742-761111).

St Bart's Megavoltage Radiotherapy 50th Anniversary Conference
September 3–5, 1987
St Bartholomew's Hospital, London
Further details: The Secretariat, Concorde Services, 10 Wendell Road, London W12 9RT

XI World Congress on Sarcoidosis and Other Granulomatous Disorders
September 6–11, 1987
Milan, Italy
Further details· PO XI WCS, Congress Studio, Via Cappuccio, 19, 20123 Milano, Italy.

1st Copenhagen Symposium on Uroradiology: Imaging and interventional techniques
September 7–10, 1987
Herlev Hospital, University of Copenhagen, Denmark
Further details· Dr Henrik S Thomsen, Department of Diagnostic Radiology 54E2, KAS Herlev, Herlev Ringvej, DK-2730 Herlev, Denmark.

XIVth Congress of the European Society of Neuroradiology
September 8–12, 1987
Udine, Italy
Further details M. Leonardi, Servizio di Neuroradiologia, Ospedale Civile, 33100 Udine, Italy

HPA Annual General Meeting and IPSM Scientific Meeting
September 15–19, 1987
Liverpool
Further details. IPSM, 47 Belgrave Square, London SW1X 8QX (Tel 01-235 6111)

Radiology and Management of Trauma Course
12–15 October, 1987
Leicester Royal Infirmary
Further details: Dr D Finlay, Consultant Radiologist, Leicester Royal Infirmary, Leicester LE1 5WW

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☐ **Review Article: The Radiological Effects of Nuclear War** (*BJR,* 1983, *56,* 147–170) 50p
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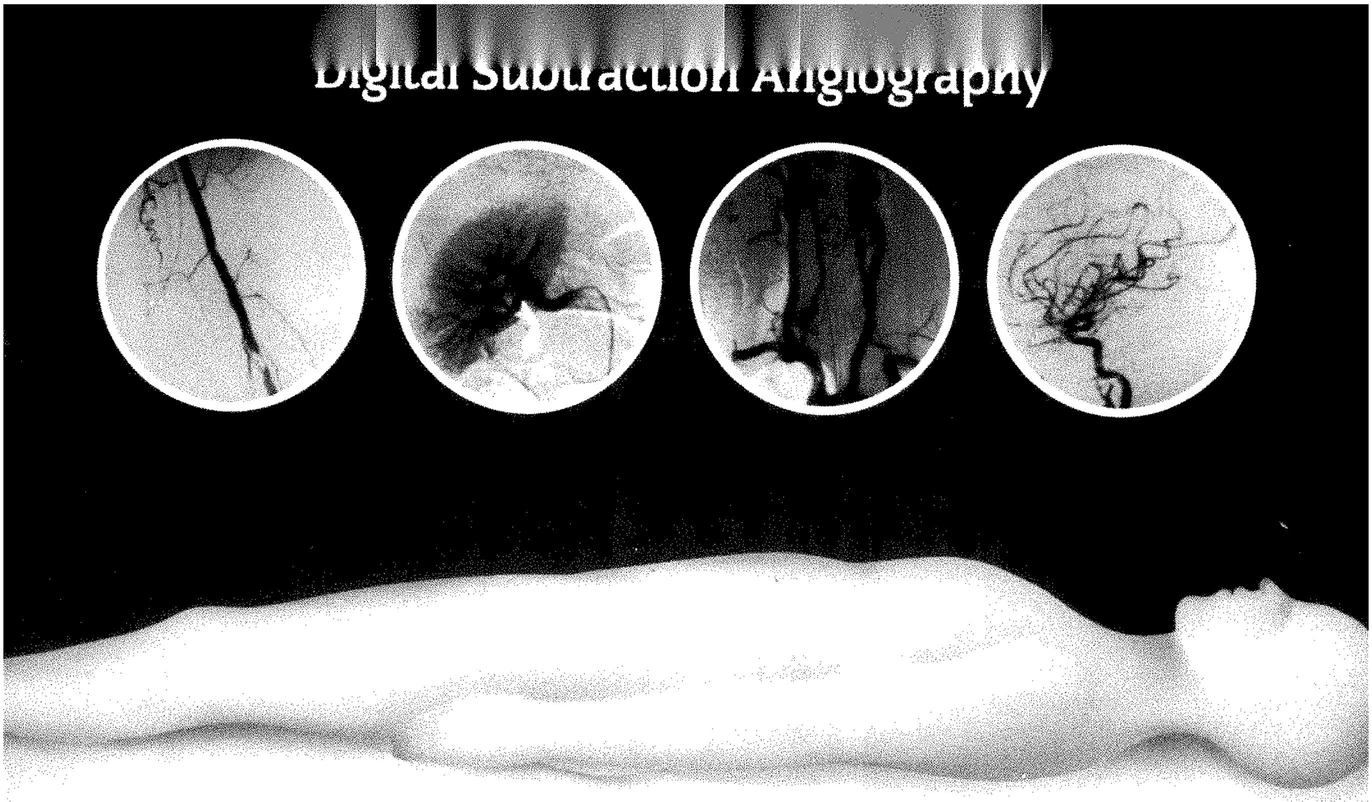

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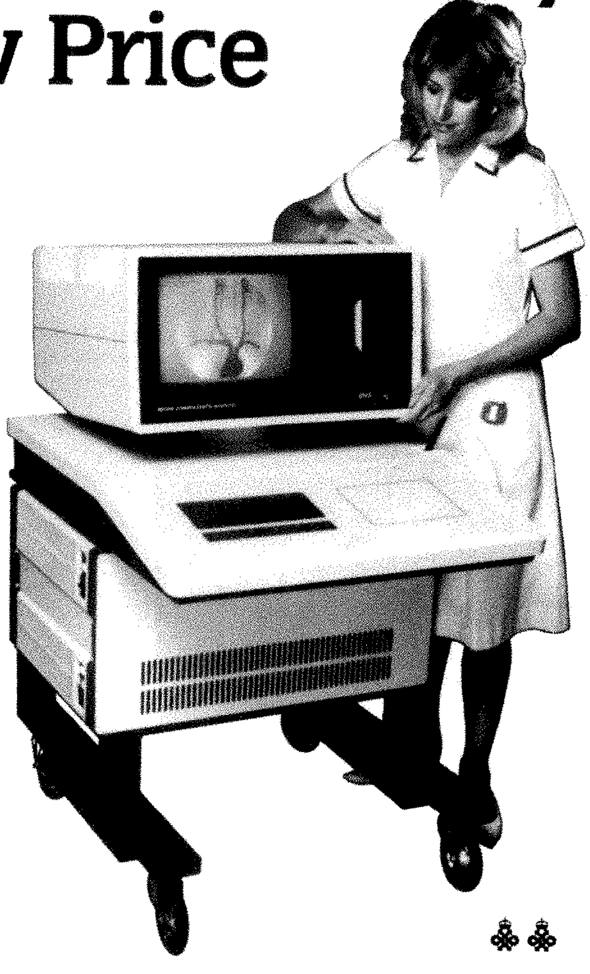

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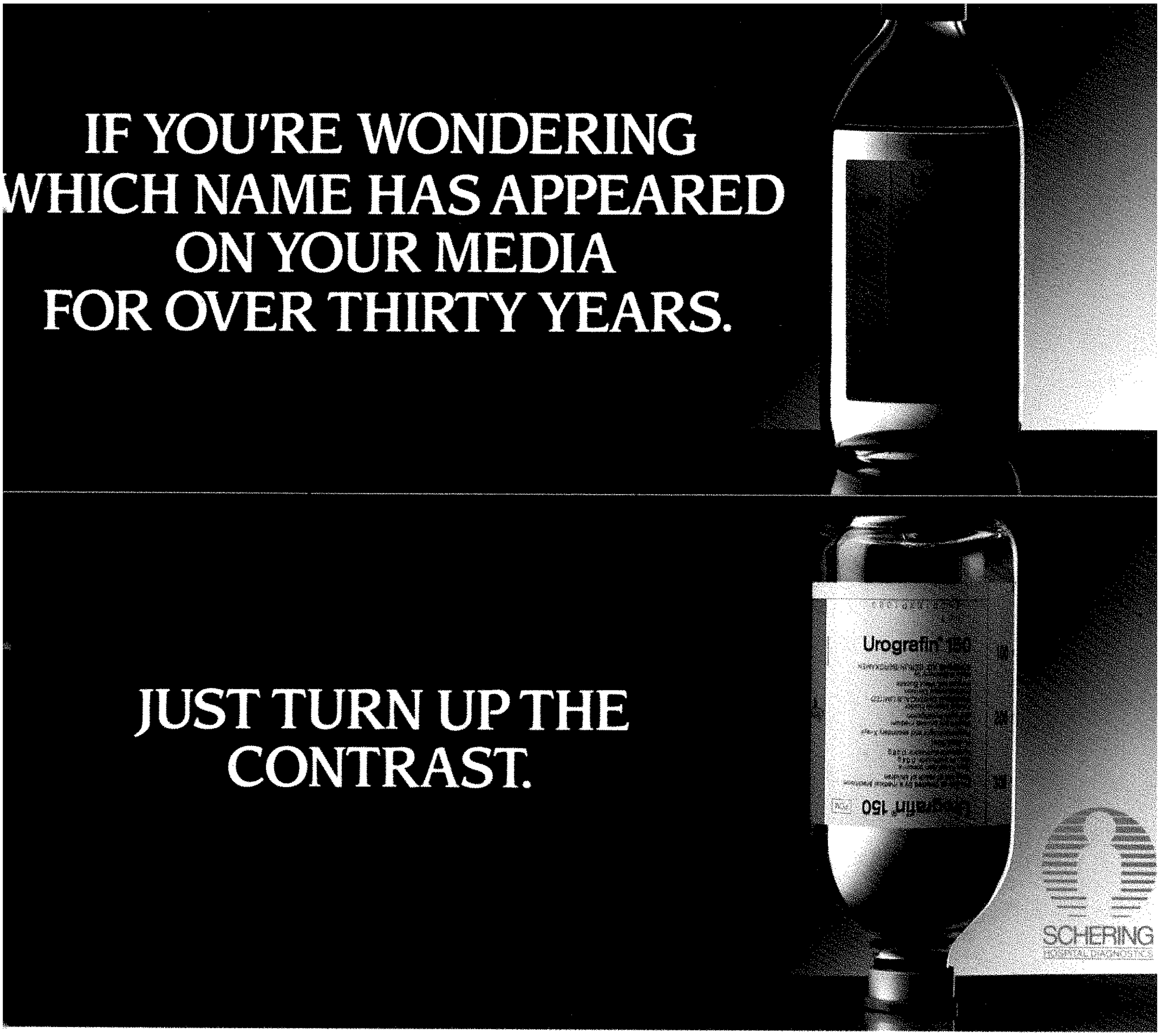

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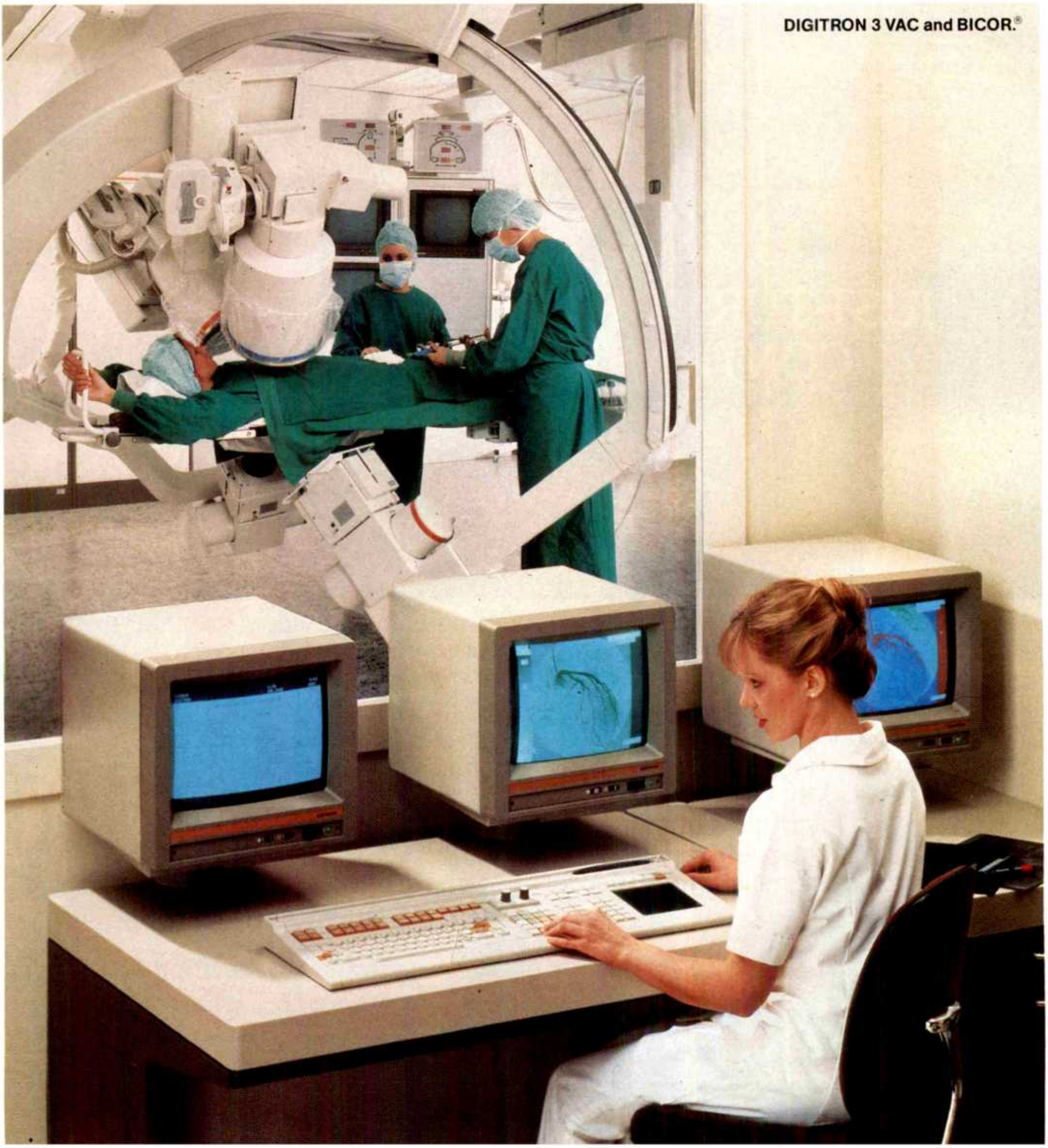

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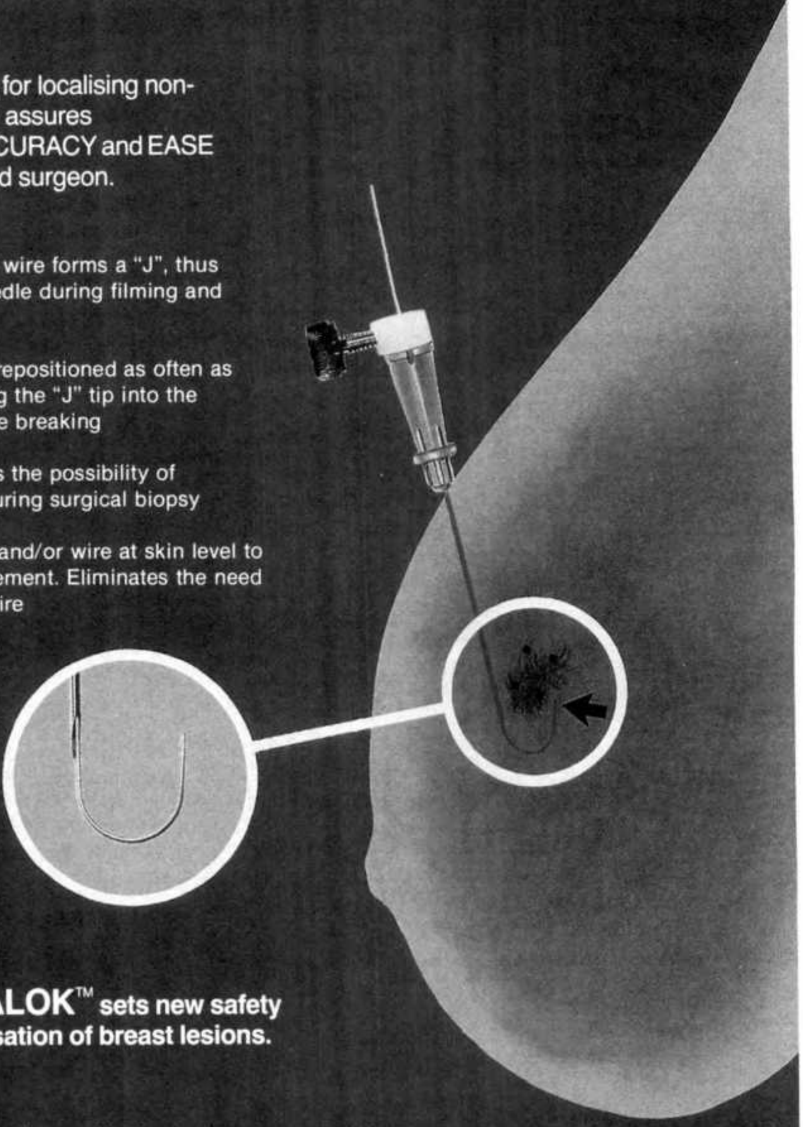

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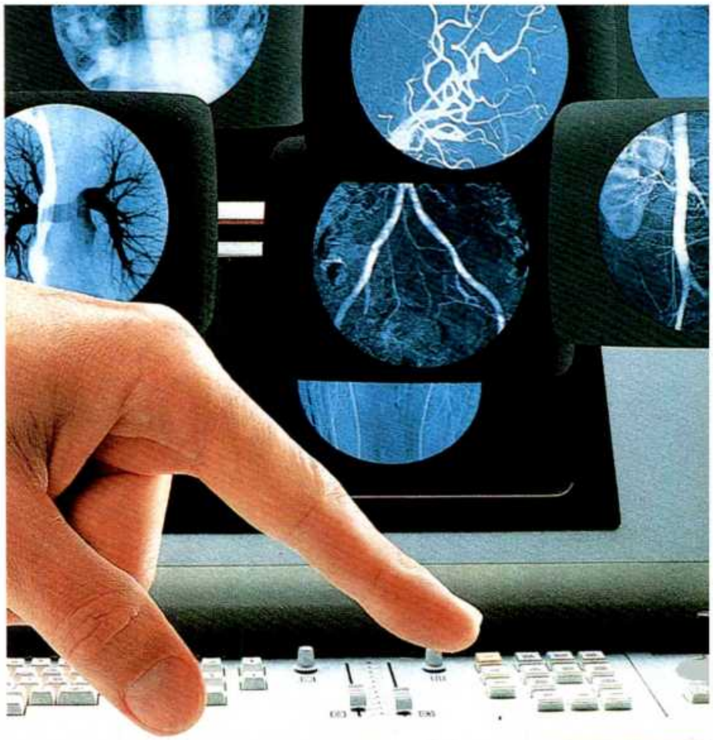

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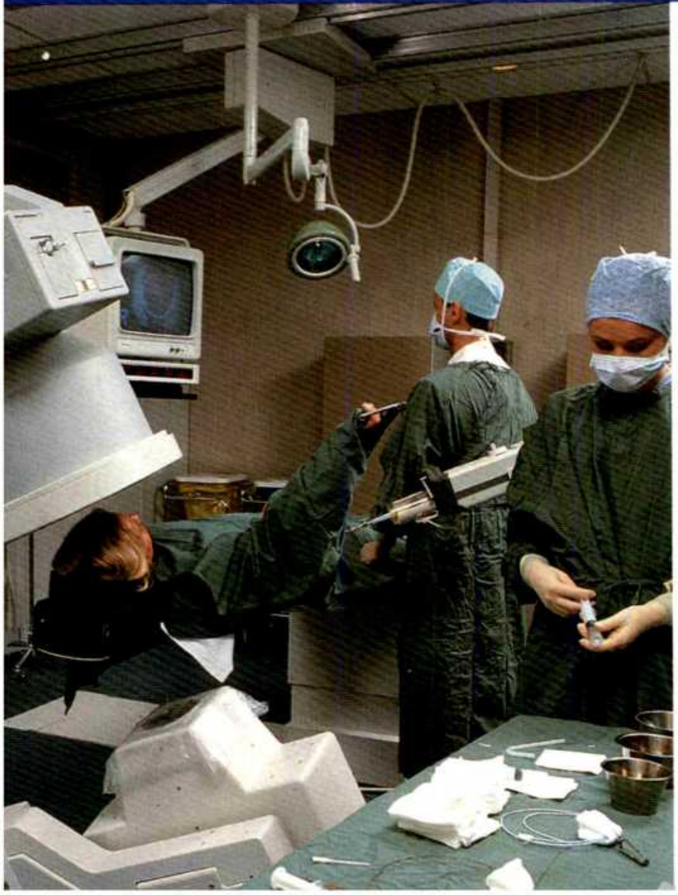

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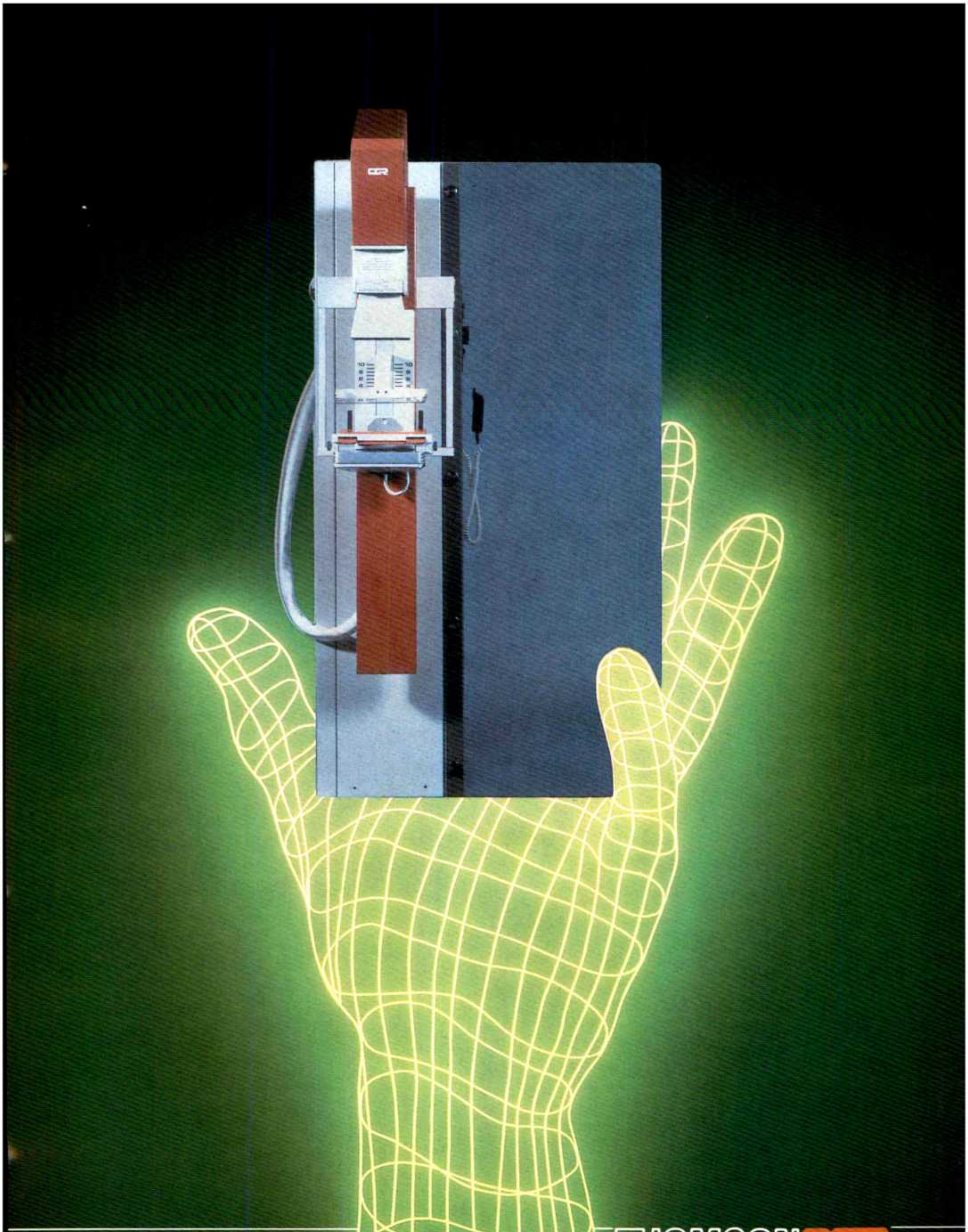
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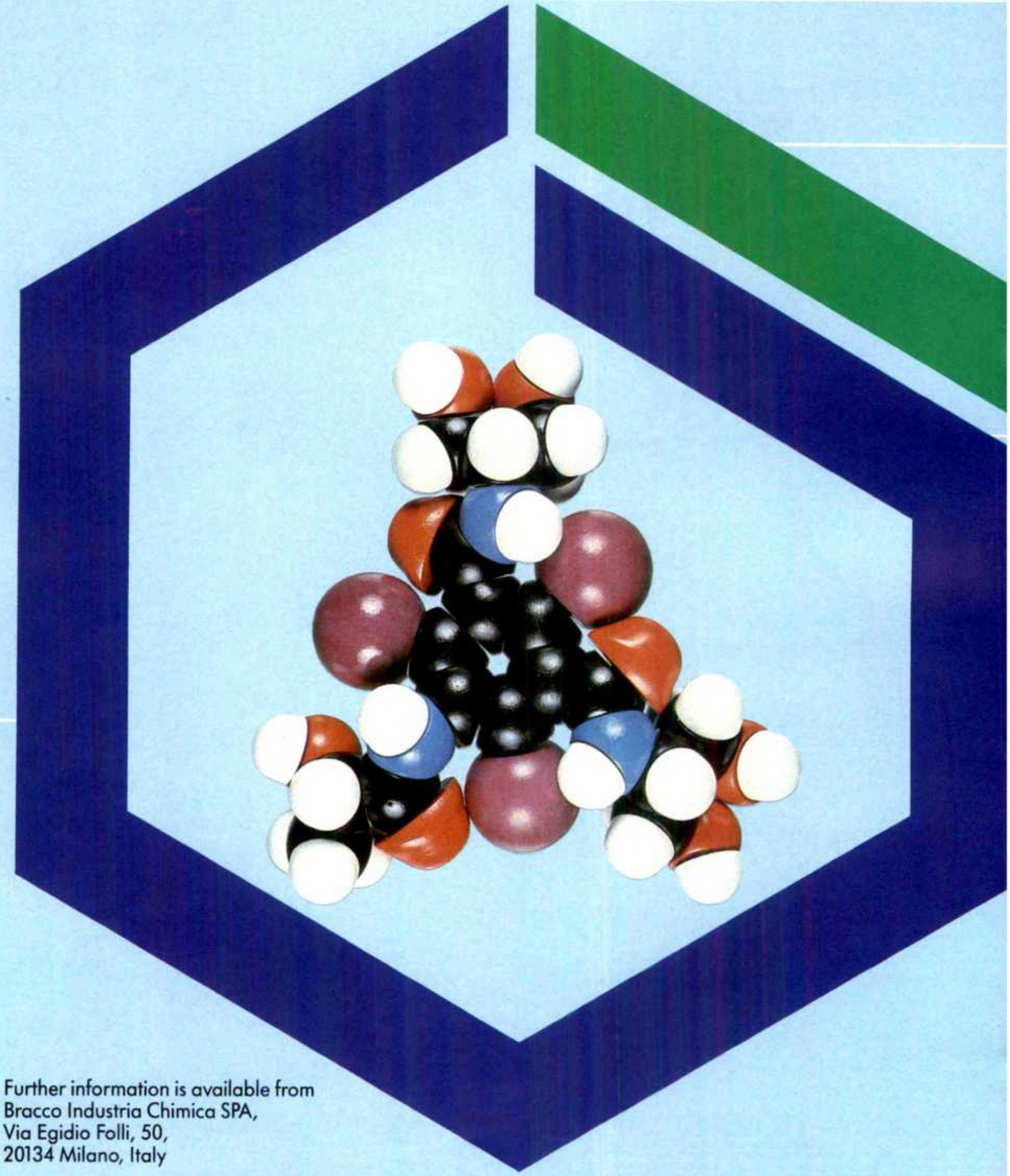

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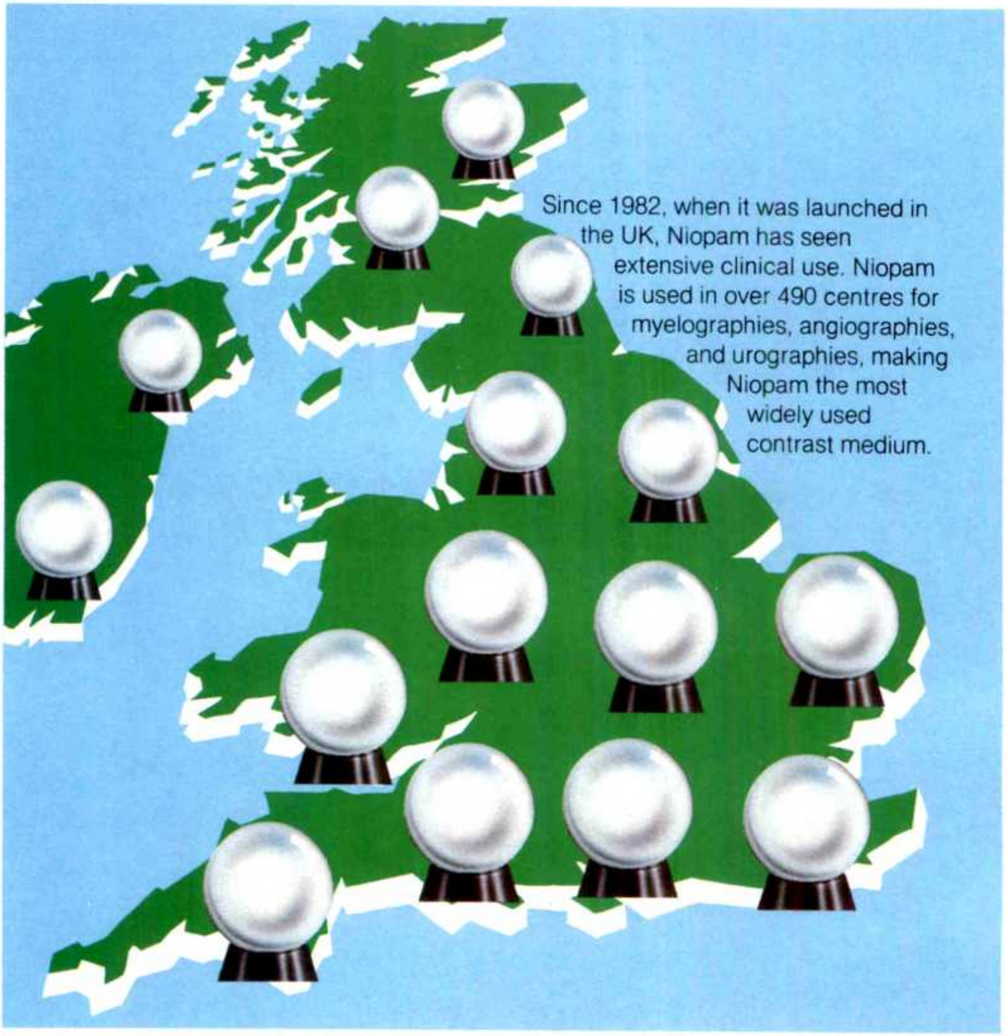

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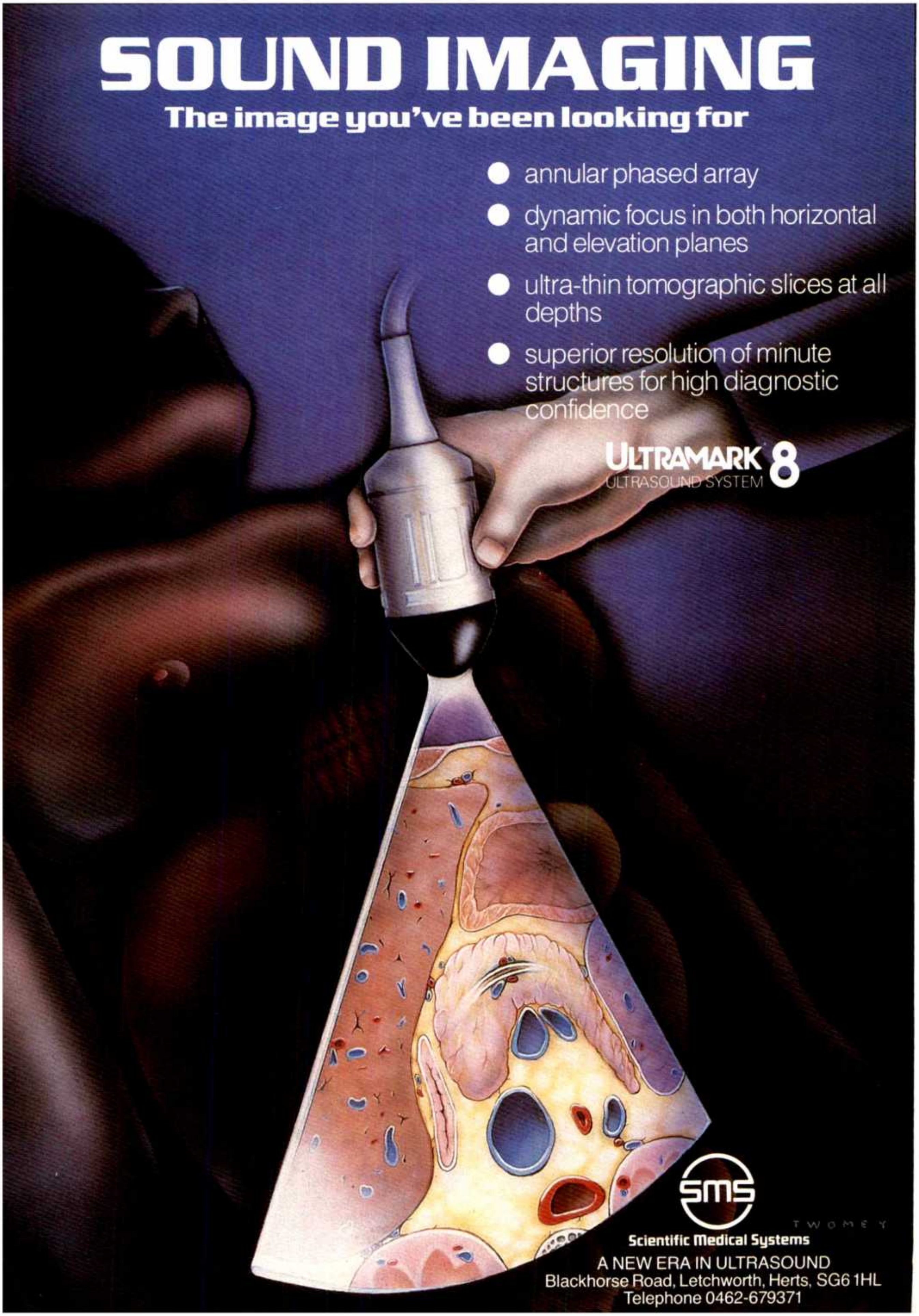

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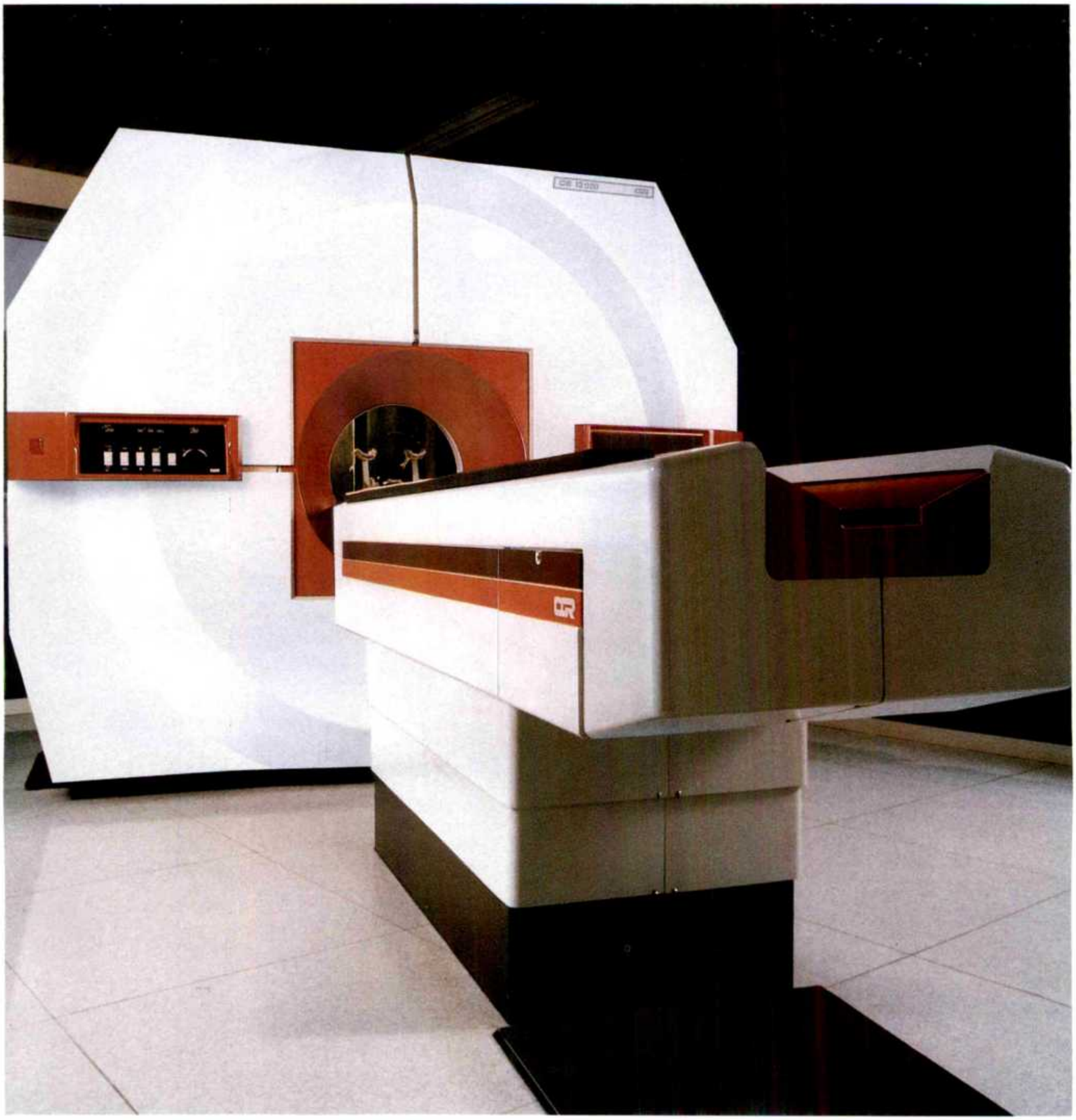

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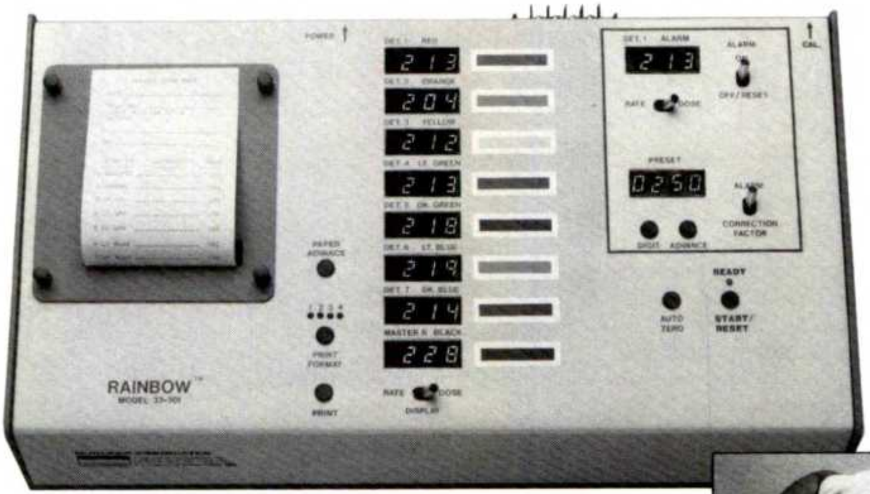

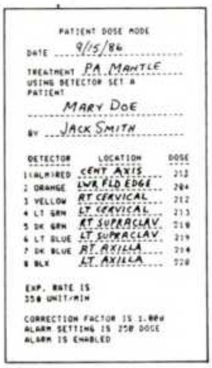

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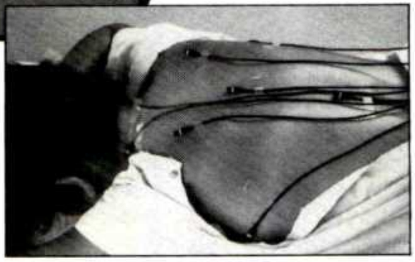

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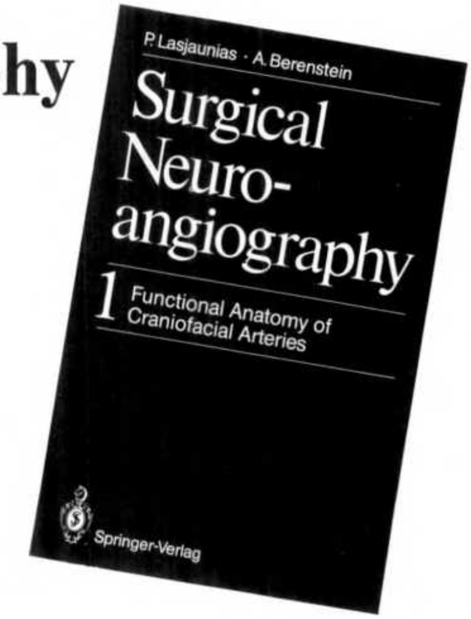

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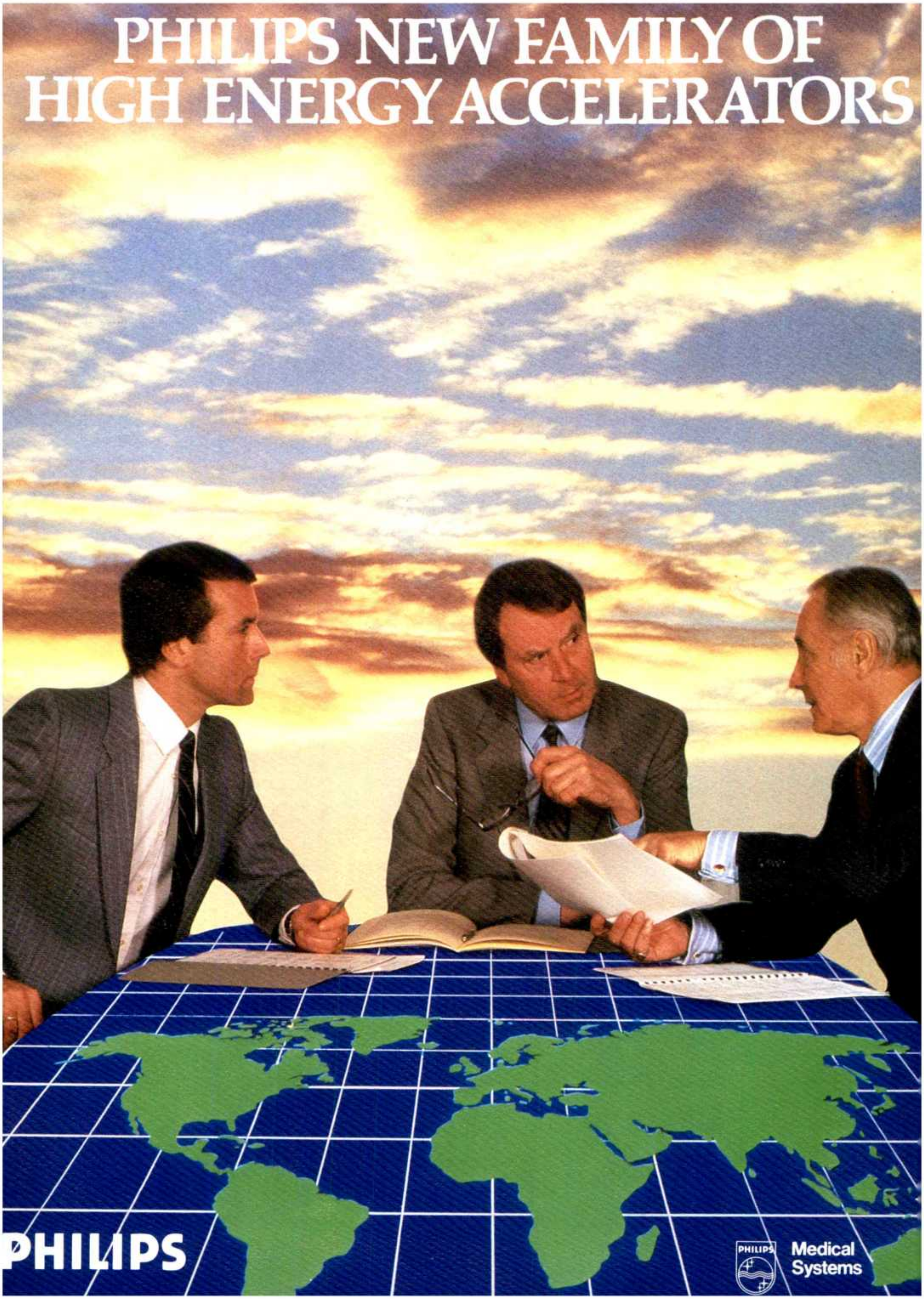

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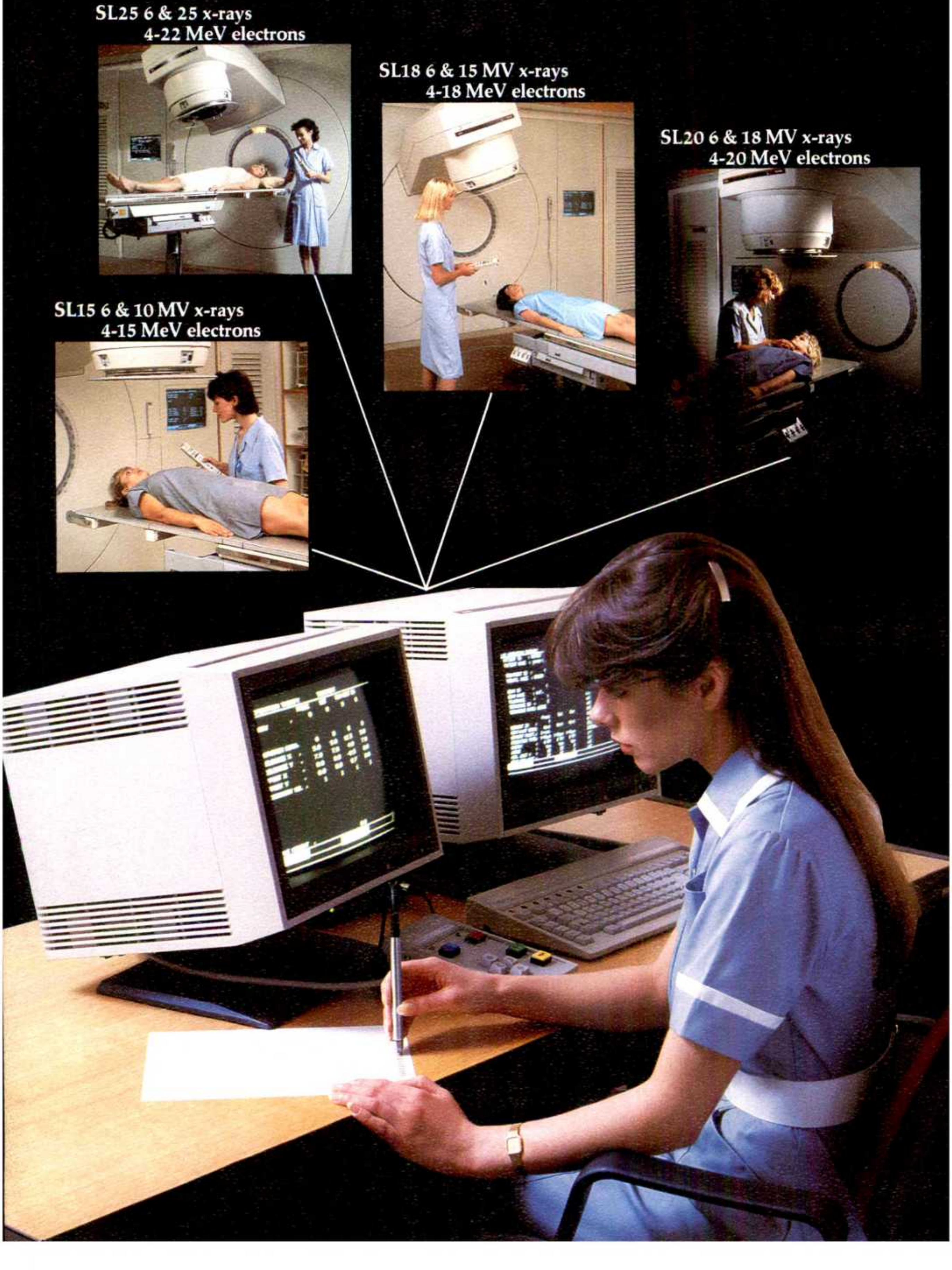

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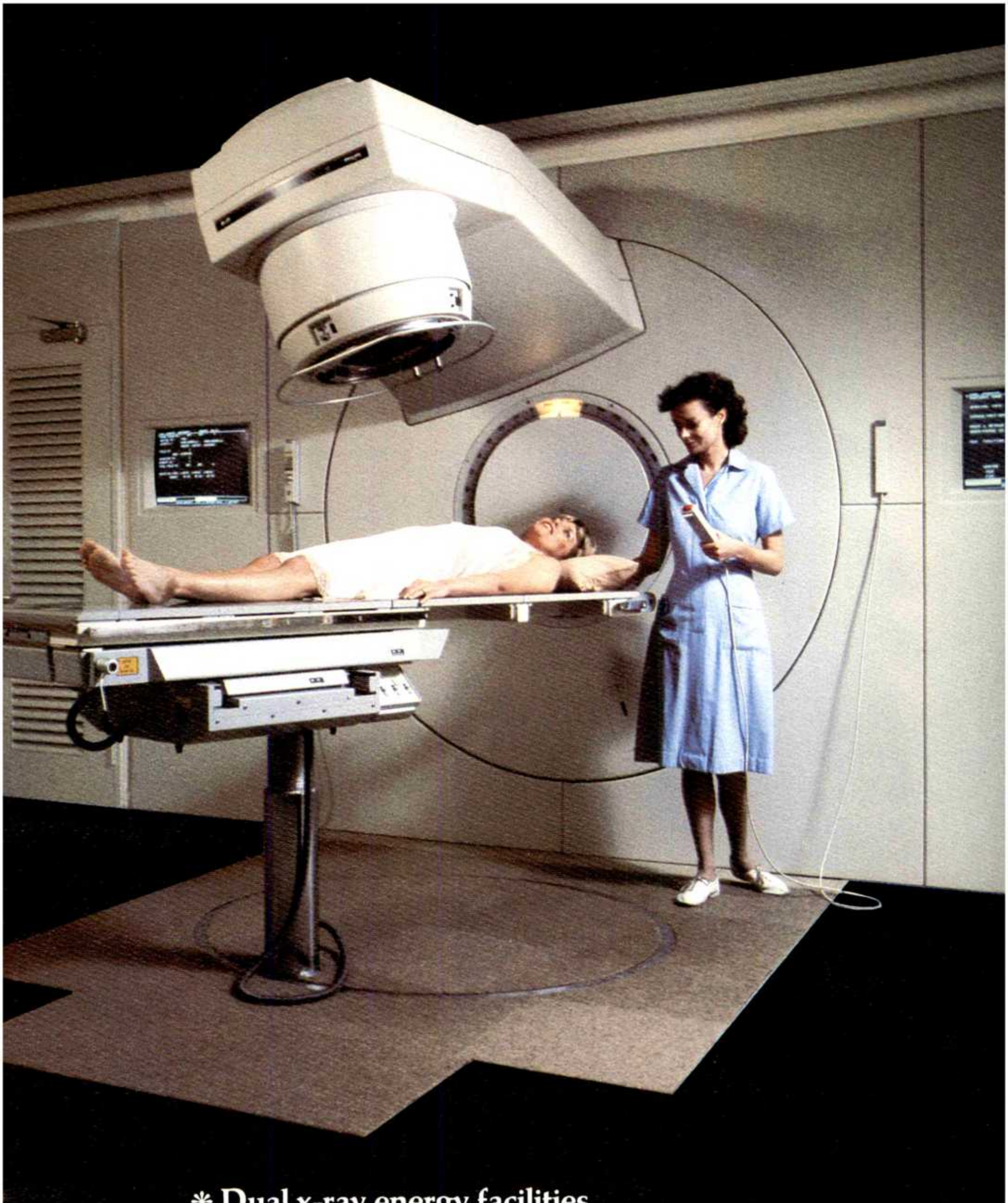

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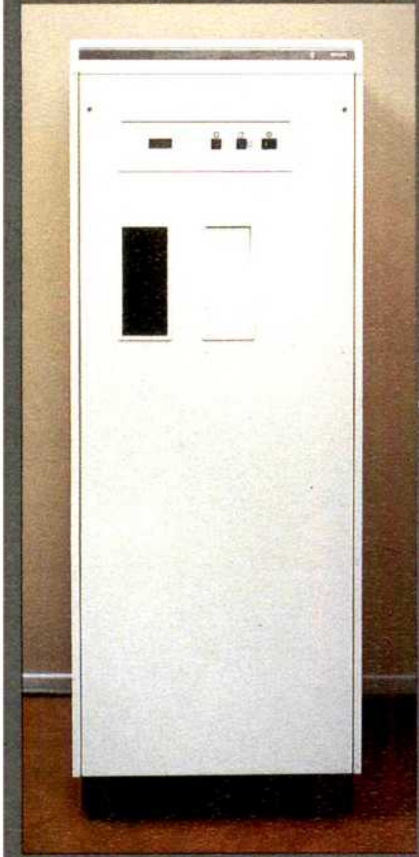

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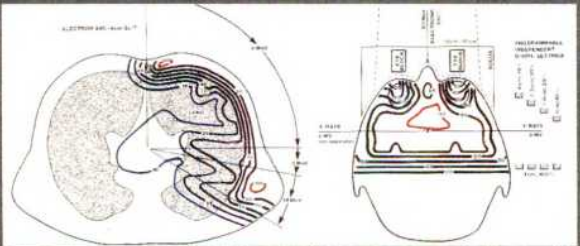

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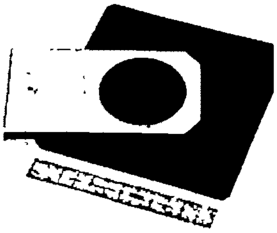

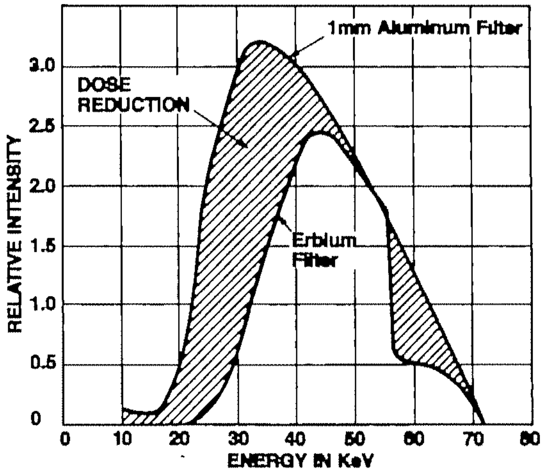

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The British Journal of Radiology

Demonstration of pulsatile cerebrospinal-fluid flow using magnetic resonance phase imaging

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(*Received March 1986 and in revised form November 1986*)

ABSTRACT

The study of pulsatile cerebrospinal-fluid (CSF) flow may be useful in diagnosis of certain forms of intracranial disease. Previous techniques used to study CSF flow either are invasive or do not allow accurate measurement. Magnetic resonance imaging (MRI) offers a non-invasive method of studying the CSF pathways. Our technique uses MR phase images and allows quantitative measurement of flow velocities and volume-flow rates. Four volunteers were studied at the level of the second cervical vertebra (C2). The MRI pulse sequence was gated from the R-wave of the subject's electrocardiogram and 12 scans were taken corresponding to different times in the cardiac cycle. The variation in flow velocity throughout the cycle was plotted, and maximum caudad and cephalad flow velocities and flow rates were calculated. Good agreement was found between three of the four volunteers. The mean maximum caudad velocity was 2.91 cm s^{-1} occurring at a mean time of 190 ms after the R-wave. This corresponds to a mean maximum flow rate of 4.13 ml s^{-1}. The total imaging time for each study was about 1 h. Technical developments, allowing simultaneous acquisition of several images throughout the cardiac cycle, will reduce this time significantly.

The cerebrospinal-fluid (CSF) pathways are particularly difficult to study, and to obtain reliable information the haemodynamic conditions must not be altered, for example, by surgical intervention. Radiologists have, for a long time, been aware of the pulsatile nature of CSF flow at fluoroscopy during Pantopaque myelography and in cineradiology of myelography and encephalography (du Boulay, 1966; du Boulay et al, 1972). Estimations of CSF flow using these techniques, which were derived from observation of a television monitor, were inevitably imprecise.

The appearance of flowing fluid using magnetic resonance imaging (MRI) has been the subject of much research, and various techniques have been developed to demonstrate the velocity of blood flow. The effects of blood flow on magnetic resonance (MR) images are dependent on the pulse sequence used, and on the velocity profile of the flow. They can be interpreted as either an increase or decrease in signal compared with stationary material (Axel, 1984; George et al, 1984). The precise variation in signal intensity as a function of velocity is dependent on many factors and is thus difficult to predict.

The nuclear magnetic resonance signal has two components which are referred to as the real and imaginary parts of the signal. These two components can be used to calculate both the modulus and the phase of the signal for each pixel. It is the modulus value that is normally used to obtain the standard clinical MR images. It has been shown, however, that phase images can also be used to quantify flow velocities (Moran et al, 1985). Whereas the modulus MR image contains information on proton density, relaxation time parameters (T_1 or T_2) and flow effects, the phase image contains information on the velocity and direction of flow, as well as phase shifts due to magnetic-field inhomogeneity, chemical shifts, and changes in magnetic susceptibility. The velocity information is usually encoded by adding extra gradient pulses into the pulse sequence (Bryant et al, 1984, Van Dijk, 1984). Alternatively, the bipolar form of gradient pulses which are part of the standard imaging sequence, such as those used for slice selection, can be exploited to provide velocity encoding (Ridgway & Smith, 1986). The range of velocities to be measured can be altered by changing the temporal separation of the two components of the bipolar pulse. Thus, peak velocities in the ascending aorta, and slower venous flow, can both be imaged using the same technique.

Pulsatile CSF flow has been demonstrated in the cerebral aqueduct and pontine cistern using MRI by showing a variation in signal intensity over the cardiac cycle (Bergstrand et al, 1985). An inversion–recovery pulse sequence was used in this study and though a cyclical variation in intensity was shown, no direct quantification of velocity or direction of flow was possible. Phase imaging has not previously been used to image pulsatile CSF flow.

The study describes the extension of a phase imaging technique which was originally developed to measure arterial flow in the body. The technique was modified to measure slow flow in the head and neck.

METHOD

This study was performed using a 0.08 T resistive MRI system manufactured by M&D Technology Ltd.

The imaging technique acquires two phase images, each having different velocity encoding, achieved by varying the temporal separation of the dephase and rephase components of the slice selection gradient (Ridgway & Smith, 1986). The final velocity image is obtained by subtracting these two images, thus eliminating any phase shifts due to field inhomogeneity, chemical shifts or changes in magnetic susceptibility. The technique was modified to image at lower velocity ranges by extending the separation of the bipolar slice selection gradients in one of the velocity-encoding pulse sequences. The difference in separation for the two pulse sequences was thus extended from 2 ms to 12 ms. The maximum measurable velocity, corresponding to a phase shift range of ±180°, was thus decreased from 120 cm s^{-1} to 20 cm s^{-1} making finer velocity resolution possible Further modifications involved the inclusion of stronger gradients and the use of a smaller-diameter RF coil, used routinely for head imaging.

The flow measurement was calibrated for mean flow velocities in the range 1–11 cm s^{-1} A simple continuous-flow phantom was used, incorporating a tube of inside diameter 10 mm, containing copper sulphate solution with $T_1 = 250$ ms. The phantom was fed from a constant head tank and mean flow rates were calculated by finding the time taken for a known volume to pass through the phantom. The MRI pulse sequence was triggered from an external source at a repetition rate corresponding to a heart rate of 75 beats min^{-1}. Each scan was repeated three times and the flow rate recorded before and after each scan.

Four volunteers were imaged, gating the pulse sequence with the subject's electrocardiogram (ECG) (Smith et al, 1986). Heart rates were monitored and images were obtained with delays of 110, 140, 165, 190, 215, 240, 290, 390, 490, 590, 690 and 790 ms after the subject's R-wave. More images were obtained during the systolic period where the velocity variation appeared to be more rapid. The total imaging time for each subject was about one hour.

Prior to this study, one volunteer was imaged at 12 levels in the head and neck at the time during the cardiac cycle when the peak velocity was attained The resultant images suggested that the peak velocity was higher in the neck than in the head. Imaging too low in the neck resulted in increasing loss of sensitivity with distance from the head coil. As a compromise the level chosen for the four volunteers was at the level of the second cervical vertebra (C2).

The mean phase shift within the ring-shaped subarachnoid space was calculated using two regions of interest, the outer represented the boundaries of the spinal canal and the inner, the spinal cord. From these two regions the mean phase shift within the subarachnoid space and its area were determined. The calibration curve was used to determine the velocity from the phase shift, and the area of the subarachnoid space was used to calculate flow.

In order to assess the reproducibility of the technique, expressed as a coefficient of variation, one volunteer was scanned six times at the same level at the time of peak velocity

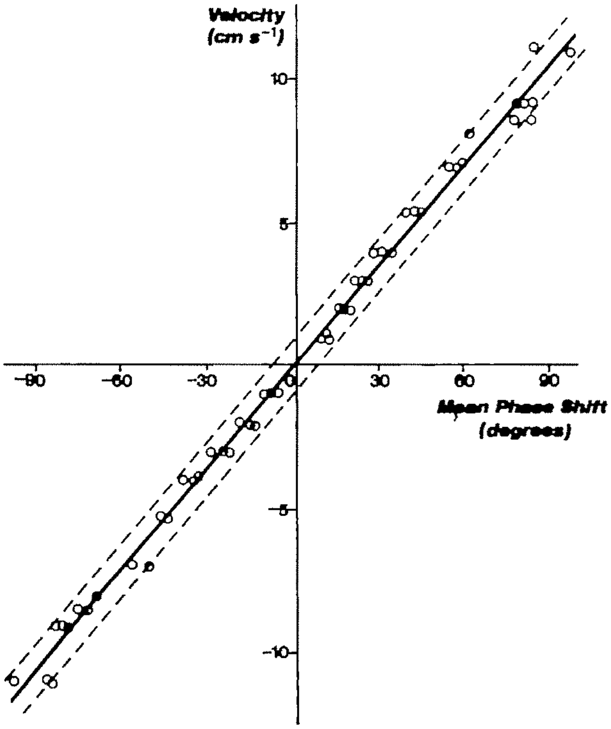

Fig 1

Calibration curve showing calculated mean velocity versus the mean phase shift. The 95% confidence limits with which velocity can be predicted from phase shift are also shown.

Results

The results of the velocity calibration are plotted in Fig. 1, showing 95% confidence limits at ±0.92 cm s^{-1}. There was a significant correlation ($r = 0.998$, $p < 0.001$) between the phase shift (degrees) and the flow velocity (cm s^{-1})

A representative transverse section from one of the normal volunteers is illustrated in Fig 2, showing both the modulus and the phase images. The CSF flow in the subarachnoid space can be seen on the phase image as a ring-shaped area. The displayed intensity of the phase image is related to velocity. Velocity in the caudad direction is represented by lighter shades of grey which correspond to a positive phase shift (Fig. 3A). Similarly, velocity in the cephalad direction is represented by darker shades of grey which correspond to a negative phase shift (Fig. 3B). Mid-grey represents zero velocity, corresponding to zero phase shift.

All volunteers demonstrated pulsatile flow within the subarachnoid space during the cardiac cycle and a representative flow-velocity curve is shown in Fig. 4.

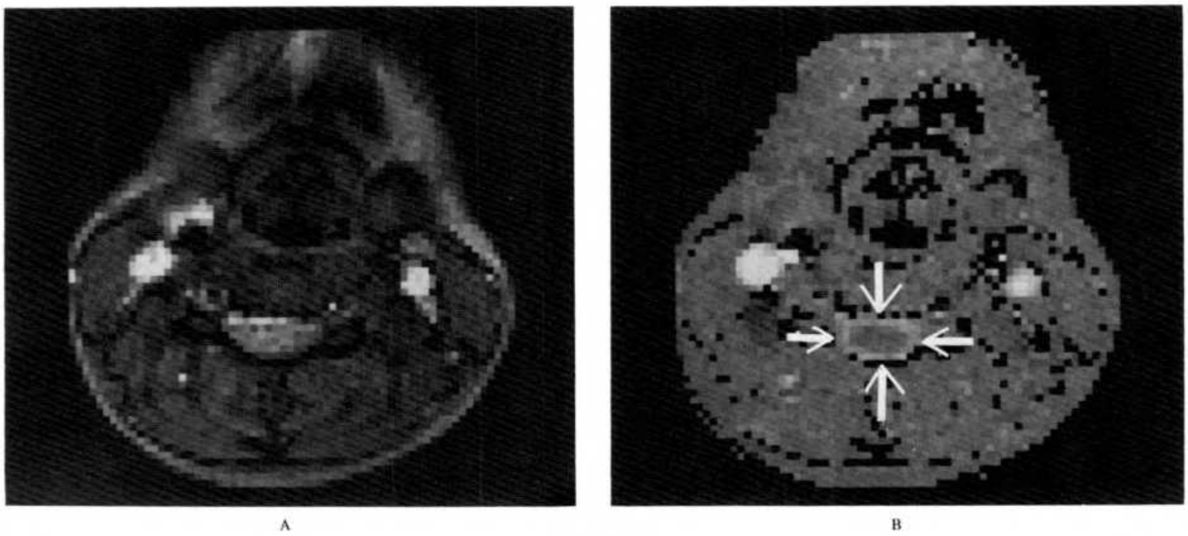

FIG. 2.

Representative section of those used in the volunteer study showing (A) the modulus image and (B) the phase image. The CSF flow is seen on the phase image as a ring of increased intensity (arrows). Also seen are left and right internal jugular veins.

Maximum flow rates, maximum flow velocities and time to peak flow for all subjects are listed in Table I. At intervening times during the cardiac cycle, flow velocities were relatively small and their corresponding phase shifts were not significantly different from phase shifts measured in adjacent soft tissue. The maximum variation in heart rate in any one volunteer was from 65 to 83 beats min^{-1}.

The reproducibility of the repeated scan, analysed once, was 14.4%. However, this figure includes the error associated with the estimation of phase information from a single image which was found to be 8.7%. The reproducibility of the technique itself is therefore 11.5%.

Discussion

This study not only confirms the ability of MRI to demonstrate pulsatile CSF flow, but also demonstrates

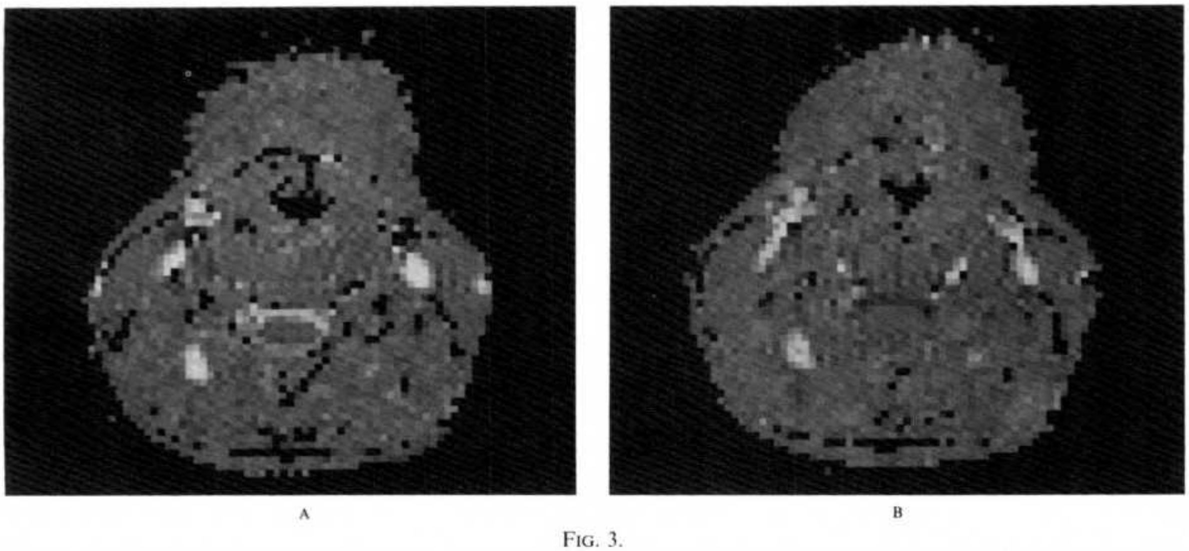

FIG. 3.

Two representative phase images demonstrating the pulsatile nature of the CSF flow: (A) shows caudad flow (positive phase shift); (B) shows cephalad flow (negative phase shift).

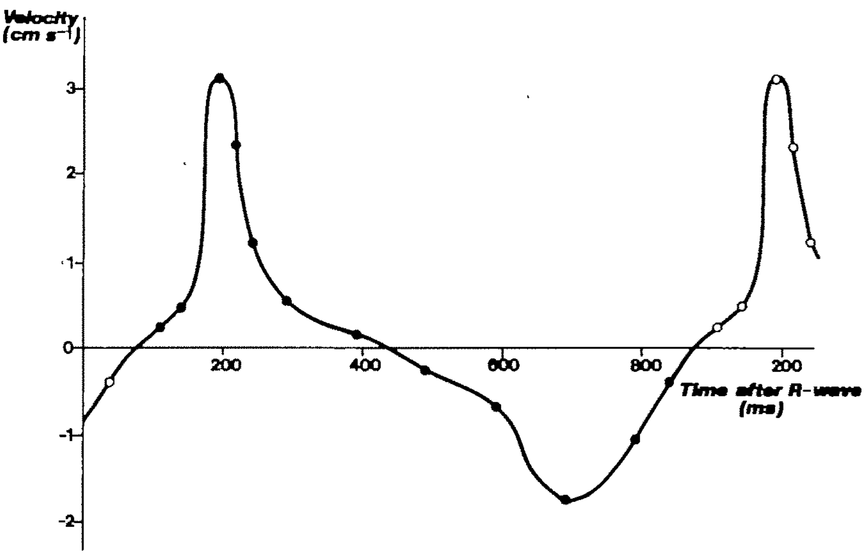

FIG 4

Variation of CSF flow velocity (cm s^{-1}) plotted against time after the R-wave (ms). The set of measured points are shown as filled circles. The same set of points was plotted (open circles) in adjacent ECG cycles to show the continuity of the curve In this case the average R–R interval was 800 ms (corresponding to a heart rate of 75 beats min^{-1})

that phase imaging enables quantitative measurement of flow velocity to be obtained with reasonable accuracy. In addition, the direction of flow can be assessed. The technique therefore has advantages over methods which rely on signal intensity (Bergstrand et al, 1985). However, unlike Bergstrand, we have been unable to demonstrate flow within the cerebral aqueduct, though this may be due, in part, to the lower signal-to-noise ratio that is obtained with the lower-field system used in this study.

There is good agreement between the flow rates and velocities obtained in three out of our four normal subjects. Shorter sampling intervals would enable these values to be established more accurately; currently the "peak" caudad and cephalad velocities could be underestimated. The variation in the time to peak CSF flow velocity may be due to many factors including the sampling time, *i.e.* time after R-wave, respiratory rate or variation in heart rate.

At present, the total imaging time for each subject is probably too long for routine clinical use. Simultaneous multislice acquisition would substantially reduce total imaging time but the spatial location of each section would be different. Alternatively, the acquisition of multiple images of a single section throughout the cardiac cycle, as has been done in cardiac imaging (Waterton et al, 1985) would also reduce imaging time.

This technique offers potential for the investigation of disorders involving the CSF circulation In the case of complete obstruction, for example, pulsation distal to the obstructing lesion will stop, but it will persist on the cranial side. In addition, du Boulay (1966), using myelographic techniques, observed that when the subarachnoid space was narrowed but not obliterated the amplitude of movement could be considerably exaggerated. Magnetic resonance imaging offers a non-invasive method of studying the direction and velocity of CSF flow in such patients.

ACKNOWLEDGMENTS

This research is generously funded by a grant from the Scottish Home and Health Department We would like to

TABLE I

MAXIMUM CSF FLOW VELOCITIES AND FLOW RATES

Subject	Max caudad flow velocity (cm s^{-1})	Max caudad flow rate (ml s^{-1})	Time of max caudad flow after R-wave (ms)	Max cephalad flow velocity (cm s^{-1})	Max. cephalad flow rate (ml s^{-1})	Time of max. cephalad flow after R-wave (ms)	Approximate mean R–R interval (ms)
1	3.17	4.41	190	1.33	1.89	690	750
2	1.78	2.44	215	1.10	1.78	110	750
3	3.57	4.71	165	1.70	2.28	690	800
4	3.12	4.96	190	1.74	2.99	690	800
Mean	2.91	4.13	190	1.47	2.24	—	775
SD	0.78	1.15	20	0.31	0.55	—	29

thank Mrs C. N Rowan for secretarial services and Mr I Lennox of the Department of Medical Illustration We would also like to thank Professor J J K Best and Dr D. M. Kean for their helpful comments and support.

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Book reviews

Basic Doppler Echocardiography Clinics in Diagnostic Ultrasound 17. Ed by J. Kisslo, D. Adams and D. B. Mark, pp. xiii + 215, 1986 (Churchill Livingstone, New York), £28.00. ISBN 0–443–08431–9

The fundamental developments of cardiac blood flow analysis by Doppler ultrasound have paralleled those of imaging, but Doppler has been slower to enter general clinical use. However, the introduction of on-line spectral analysers and demonstration of the ability to measure transvalvar pressure gradients with accuracy equal to that of cardiac catheterisation, have stimulated enormous interest in the method and most machines currently purchased for cardiac applications are now of the "duplex" type, with facilities for pulsed-wave (PW) and continuous-wave (CW) Doppler There is, thus, an undoubted demand for a book which, as its Preface states, aims to provide a simple and straightforward introduction for beginners to Doppler echocardiography.

The opening chapters explain the physical principles of PW and CW Doppler and the methods used to record flow data Use of the machine controls is covered in detail, but with reference to only one particular machine and nothing, for example, about high-pass filters, mean or modal velocity estimators or high PRF systems The examination technique is comprehensive, but assumes a firm background in two-dimensional cardiac imaging

The second half deals with clinical applications. Valve stenosis and regurgitation are treated well The chapter on ventricular function is short on practical advice needed by a beginner, for example how to trace the ejection velocity contour. Paediatric applications are poorly covered. The need for a chapter on fetal blood flow in a book for beginners is questionable.

Most of the illustrations and explanatory diagrams are helpful, but some photographs are out of focus. My major criticism is the prose style which, even allowing for trans-Atlantic differences, is long-winded and replete with jargon, something to be avoided in a book for newcomers Firm editing could reduce the text by 30% and make the arguments much easier to follow.

The authors have wide experience of this new and exciting field and their effort to disseminate it is laudable. A little more self-discipline would have satisfied much better the need they have rightly perceived

GRAHAM J. LEECH

Digital Subtraction Angiography: Practical Aspects. By A. van Breda and B T Katzen, pp 230, 1986 (John Wiley and Sons Ltd, Chichester), £34.95

ISBN 0–943432–60–X

As indicated by its title, this book is essentially a practical account of the capabilities and techniques of digital subtraction angiography (DSA). In addition to the chapters by the main authors there are contributions from a cardiologist, a radiographic technician and a nursing supervisor. Discussion covers the practical aspects of both intravenous and intra-arterial DSA of the various regions, including its value in interventional angiography Consideration is also given to the implications that the mixed outpatient and day-patient population may have on the department, particularly with regard to patient preparation and after care. Emphasis is placed on the quality and value of "day case" intra-arterial studies, a technique considerably enhanced by the advent of high-flow, small-diameter catheters

Each chapter is followed by references, mostly drawn from the American literature. Illustrations throughout the book are quite clear, although two illustrations have been incorrectly orientated There are a number of minor and a couple of major printing errors which should have been avoided. Because this is a practical account of techniques, there is little critical analysis in a scientific form of the usefulness and the limitations of DSA. this would have enhanced the usefulness of the book.

Having accepted the drawbacks of the book, however, it would make useful reading for all members of a department which is envisaging the installation of a DSA unit.

R. A. FAWCITT

1987, *The British Journal of Radiology*, 60, 429–438 MAY 1987

Upper gastrointestinal endoscopic ultrasonography in gastroenterology

By P. J. Shorvon, M.R.C.P., W. R. Lees, F.R.C.R., R. A. Frost, M.R.C.P., F.R.C.R. and P. B. Cotton, F.R.C.P.

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(*Received August 1986*)

ABSTRACT

Endoscopic ultrasound is a new technique in which high-frequency, high-resolution real-time ultrasound images are obtained from within the gastrointestinal tract by use of an ultrasound probe incorporated into the tip of a fibreoptic endoscope. Forty patients were scanned for gastrointestinal indications In six patients the scans were technically unsuccessful, in three of these because of difficulties with the prototype instrument. New information was obtained in 20 patients, later confirmed by other means in 12 Endoscopic ultrasound did not provide any new information in 14 patients. The technique shows considerable promise in patients with pancreatic disorders and gut-wall malignancies It has the ability to provide images with a spatial resolution unobtainable by other imaging methods.

The practice of gastroenterology has been revolutionised by the introduction of new imaging methods over the last 15 years, not least by fibreoptic endoscopy for mucosal disease and by real-time ultrasound scanning in biliary and pancreatic disorders Recently, these two diverse imaging methods have been merged in a new technique termed endoscopic ultrasound (EUS) (Cotton et al, 1985). Specially adapted endoscopes have been constructed in which an incorporated ultrasound probe produces real-time ultrasound images from within the gastrointestinal tract. This circumvents both intraluminal gas and the bony skeleton, normally absolute barriers to ultrasound imaging, and allows the use of relatively high-frequency, high-spatial resolution transducers because of the close proximity of areas of interest. Early reports from Europe (Tio & Tytgat, 1984), Japan (Tanaka et al, 1984), and the United States (DiMagno et al, 1982, Rifkin et al, 1984), have been enthusiastic. We present our initial experience and review the literature.

EQUIPMENT

We used the Olympus ultrasonic endoscope (prototype III). This consists of a 7.5 MHz ultrasound mechanical sector-scan transducer housed in an oil-filled chamber at the tip of a specially adapted fibreoptic endoscope. The crystal is rotated at 10 cycles/s by a motor drive encased in the shaft of the endoscope. The signal from the transducer is transferred electronically down the shaft of the endoscope to a digital scan converter, and a real-time 180° grey-scale sector image is displayed. The image can be rotated electronically 45° either side, giving a total display field of 270°. The maximum depth of the display is 10 cm, and the image can be magnified up to twice life size. Facility for freeze-frame, video recording and polaroid or 35 mm slide recording is incorporated. The 13 mm-diameter endoscope is fully functioning, with light and viewing fibreoptic bundles (70% oblique viewing to axis of shaft), air and water suction and blowing channels, and a further smaller channel for infusion of water, but no biopsy channel A rubber balloon can be placed over the oil chamber and distended with deaerated water through a separate channel for acoustic coupling and standoff. Full tip deflection of the endoscope is possible using standard endoscopic controls but the presence of the transducer has resulted in an increase in the length of the rigid tip of the endoscope size to 45 mm.

A variety of designs has been produced by other manufacturers, some utilising linear-array transducers (DiMagno et al, 1982; Lutz et al, 1983, Rifkin et al, 1984)

METHODS

Any mucosal lesion is first examined by routine upper gastrointestinal endoscopy and biopsies taken as necessary. Endoscopic ultrasound is carried out in a similar manner to standard upper gastrointestinal endoscopy with the same minimal risks by an endoscopist experienced in the use of side-viewing endoscope techniques.

The patient is sedated, given pharyngeal local anaesthesia, and placed in the left lateral position. After introduction of the endoscope to the desired position under direct vision, intraluminal gas is aspirated. Direct apposition of the endoscope to mucosa may give sufficent acoustic coupling for scanning, but normally it is necessary to distend the balloon with deaerated water. In the stomach, the lumen can also be filled with deaerated water. As the stomach is a mobile organ with an inconstant relationship to surrounding structures except at its points of fixation, orientation of the ultrasound image is inferred from landmarks identified

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on the image as well as from the distance of the tip of the instrument from the teeth. If difficulty is encountered, further help can be obtained by using a conventional ultrasound probe externally to identify the tip of the instrument, either by visualising the distended balloon or by observing "crosstalk" between the two transducers. The duodenum and oesophagus are relatively fixed in position, and orientation of the image is easier from within these structures.

Mucosal lesions can be identified visually before scanning. Organs surrounding the upper gastrointestinal tract can be scanned by placing the transducer just beyond the area of interest and slowly withdrawing while rotating the endoscope back and forth, observing the ultrasound image until landmarks are recognised. Any area can be scanned in different planes by rotation and tip deflection, although the freedom of scanning lesions in orthogonal planes (generally available in conventional external ultrasound imaging) is often not possible. The entire pancreas can be examined by a combination of transduodenal and transgastric scanning. The gallbladder, common bile duct, upper abdominal aorta, cranial parts of both kidneys, left adrenal gland, adjacent parts of the spleen, and right and left lobes of liver can be scanned reliably by this method (Lux et al, 1982). Comprehensive scanning of the entire mucosa of the upper gastrointestinal tract and surrounding organs was not attempted on each patient; instead, scans were confined to the area of interest defined before the procedure. Data were collected prospectively.

PATIENTS

Forty patients have been scanned for gastroenterological indications.

Oesophagus

Six patients were scanned for oesophageal symptoms. Three had biopsy-proven oesophageal cancer for staging, two had oesophageal strictures of unknown aetiology for diagnosis, and one had a benign oesophageal stricture being considered for endoscopic diathermy to assess wall thickness.

Stomach

One patient with known gastric lymphoma was examined to assess the extent of involvement.

Duodenum

One patient with suspected duodenal varices was scanned to confirm the diagnosis.

Pancreas

Thirty patients were scanned for pancreatic indications. Eighteen patients were suspected of having a pancreatic lesion but previous imaging had produced negative or equivocal results. Twelve had a known pancreatic lesion but further information on the lesion was required.

Biliary tree

Two patients with suspected extrapancreatic biliary obstruction were scanned to determine the nature of the obstructing lesion.

RESULTS

Introduction of the endoscope was achieved in all patients. Scans were considered successful if the organs of interest were scanned and if previously known abnormalities were confirmed, or new abnormalities detected.

Oesophagus

New findings were detected by EUS in all patients with oesophageal disease. These were confirmed at surgery in two (Table I), but not independently substantiated in the other four (Table II).

TABLE I

PATIENTS WITH KNOWN OESOPHAGEAL DISEASE IN WHOM EUS PROVIDED USEFUL NEW INFORMATION, LATER SUBSTANTIATED

Reason for investigation	Previous imaging	Findings on EUS	Confirmation
1 Known carcinoma of oesophagus. Operability?	CT suggested mass extending beyond oesophagus and adherent to descending aorta	Tumour seen to extend through mucosa and muscle layer but only minimal extension into mediastinum. Less extensive than on CT. Conclusion: operable (Fig 1)	Surgery: tumour resected
2 Known carcinoma of oesophagus. Resectable?	—	Tumour confined to mucosa and no enlarged lymph nodes detected. However, lower end of tumour could not be traversed by endoscope so not all of tumour and mediastinum scanned. Conclusion: tumour resectable but scan incomplete	These limited findings were confirmed at surgery: tumour resected

TABLE II

PATIENTS WITH KNOWN OESOPHAGEAL DISEASE. NEW ABNORMAL FINDINGS CONSIDERED IMPORTANT BUT NOT INDEPENDENTLY SUBSTANTIATED

Reason for investigation	Previous imaging	Findings on EUS	Follow-up
1 Known oesophageal carcinoma. Operability?	CT: poor quality. Much artefact	Extensive infiltration of tumour into mediastinum encasing descending aorta. Conclusion: inoperable	Palliative intubation only
2 Previous distal oesophagectomy for gastric carcinoma. Stricture but no mucosal abnormality on endoscopy. Nature of stricture?	Too breathless for adequate CT scan	Multiple enlarged lymph nodes compressing oesophagus above level of anastomosis (Fig. 2)	Radiotherapy: improvement in dysphagia
3 Past history of follicular lymphoma thought to be in remission. Patient presented with lower oesophageal stricture resistant to dilatation. Endoscopy: no mucosal abnormality. Nature of stricture?	Ultrasound 1 month earlier reported as normal	Enlarged lymph nodes indenting splenic vein, in peripancreatic and para-aortic positions. Similar masses seen compressing lower oesophagus (Fig. 3)	Further chemotherapy planned
4 Recurrent peptic stricture above hiatus hernia, resistant to dilatations. Safe for endoscopic diathermy incision?	—	Thickness of oesophageal wall and surrounding fibrosis estimated to be 1 cm and safe for diathermy	Successful endoscopic diathermy of stricture without complication

Stomach

The patient with known gastric lymphoma was shown to have thickened gastric wall with loss of the five layers normally resolved by endoscopic ultrasound. The process was seen to be confined to the lower stomach, a finding confirmed histologically following gastrectomy.

Duodenum

The patient with suspected duodenal varices presented with recurrent gastrointestinal bleeding, and previous endoscopy had demonstrated telangiectasia in the stomach and proximal small bowel, and apparent extrinsic compression of the duodenal bulb. No varices were seen by EUS, but an unsuspected calcified stenotic aortic valve was noted (Fig. 4). In view of the known association between aortic stenosis and gastrointestinal bleeding (Cody et al, 1974), the patient underwent prosthetic valve replacement and has had no further haemorrhage.

Pancreas (Fig. 5)

Of the 18 patients with suspected pancreatic disease but with negative or equivocal imaging, scans were

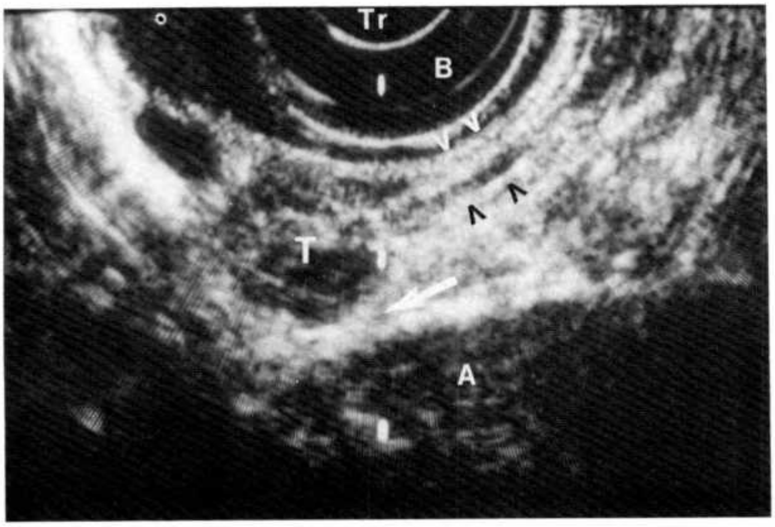

FIG. 1.

Transoesophageal scan of oesophageal carcinoma (Table I, Case 1). The small tumour (T) can be seen to extend through the oesophageal wall (arrowheads) but not deeply into the mediastinum. The fat plane between the aortic arch (A) and oesophagus is preserved (arrow). Conclusion: tumour resectable. Markers: 1 cm. Tr = transducer, B = balloon around transducer.

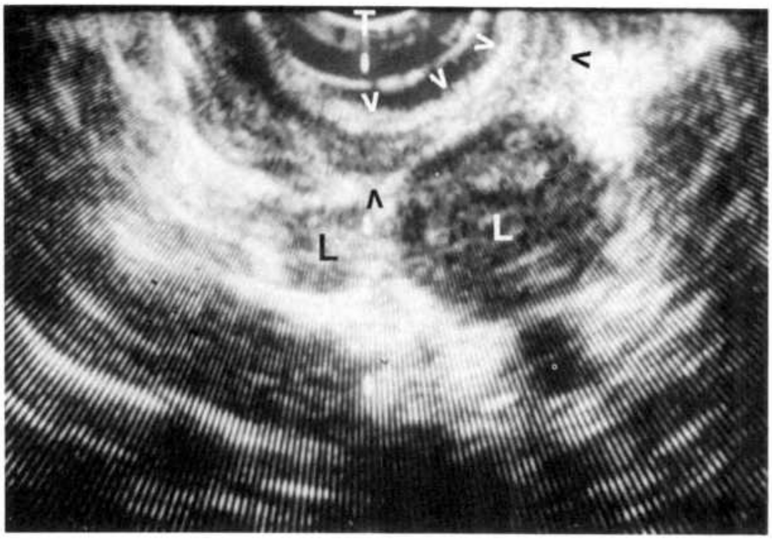

FIG. 2.

Transoesophageal scan at site of oesophageal stricture (Table II, Case 2). This patient, who had undergone previous resection of gastric carcinoma, had an oesophageal stricture with no mucosal abnormality. The scan demonstrated extrinsic compression by several nodes, two of which are seen on this scan (L). Markers: 1 cm. T = transducer, arrowheads = oesophageal wall.

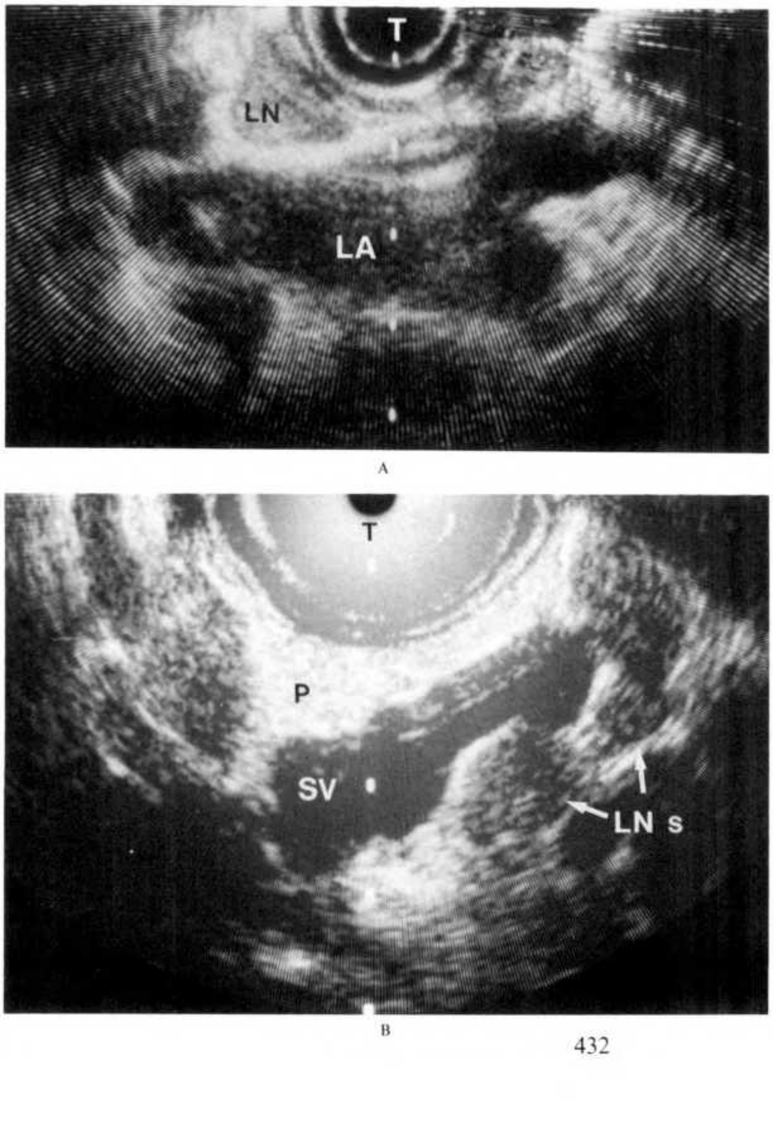

FIG. 3.

(A) Transoesophageal scan and (B) transgastric scan of a patient with a past history of follicular lymphoma. In the region of an oesophageal stricture enlarged lymph nodes could be visualised compressing the oesophagus, and further enlarged lymph nodes were seen in the abdomen. Markers: 1 cm. T = transducer, LN = lymph node, LA = left atrium, P = pancreas, SV = splenic vein.

technically unsuccessful in two patients, one because of machine failure. No new information was provided in 10. In six patients important new information was provided by EUS, confirmed by later findings in three (Table III), and still unconfirmed in the other three (Table IV).

Of the 12 patients with known pancreatic disease, important new information was provided by EUS in five patients, later substantiated in four (Table V). The fifth patient suffered chronic abdominal pain and an endoscopic retrograde pancreatogram demonstrated a mildly dilated pancreatic duct, possibly age-related. Endoscopic ultrasound confirmed the dilated duct, which was irregular with clubbing of side branches, and the surrounding pancreatic parenchyma was heterogeneous with peripheral areas of low echogenicity (Fig. 9), features of chronic pancreatitis. In four patients, scans were successfully performed but provided no new information. In the other three cases, the scans were technically unsuccessful because of balloon failure in one, failure to enter the duodenum in a patient who had undergone previous gastric surgery, and because of an unusual stomach position in another patient post-operatively.

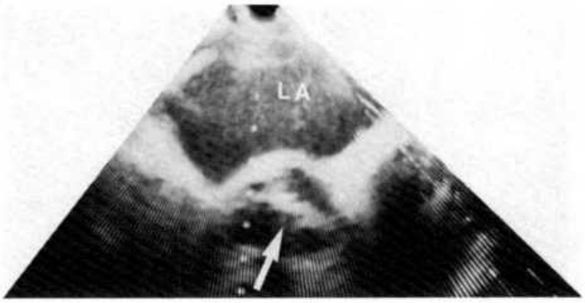

FIG. 4.

The aortic valve (arrow), scanned through the left atrium (LA), was noted to be heavily calcified. This serendipitous finding explained the patient's occult gastrointestinal bleeding. Markers: 1 cm.

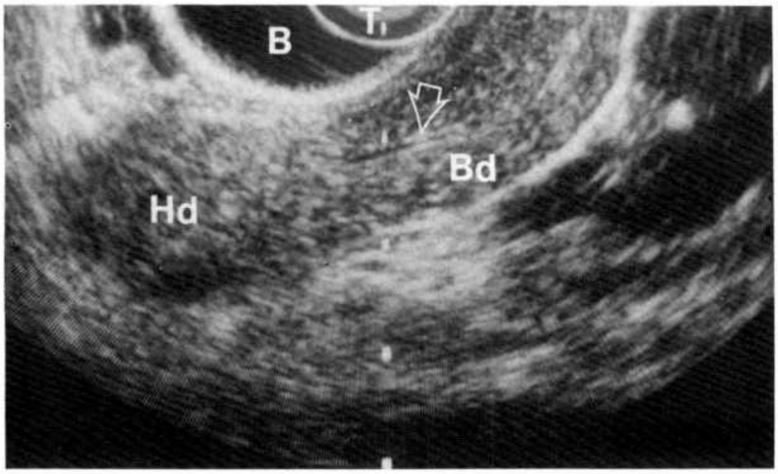

FIG. 5.

Transgastric scan of the head (Hd) and body (Bd) of a normal pancreas. Note that a section of the pancreatic duct, measuring about 1 mm, is included (arrow). Markers: 1 cm. B = balloon around transducer (T).

TABLE III

PATIENTS WITH SUSPECTED PANCREATIC DISEASE IN WHOM EUS PROVIDED USEFUL INFORMATION, LATER SUBSTANTIATED

Reason for investigation	Previous imaging	Findings on EUS	Confirmation
1 Pancreatic-type pain	ERCP: failed cannulation of accessory papilla in pancreas divisum anomaly	Dilated dorsal pancreatic duct	Surgery: chronic pancreatitis of dorsal pancreas
2 Bile duct obstruction	CT: head of pancreas mass. Ultrasound: no mass	Small cholangiocarcinoma at liver hilum; no liver metastases (Fig. 6)	Surgery
3 Suspected insulinoma	CT/ultrasound: no abnormality	Low-echogenicity tumour in tail of pancreas with coeliac and peripancreatic lymph-node metastases. Liver normal (Fig. 7)	Surgery

ERCP = endoscopic retrograde cholangiopancreatography.

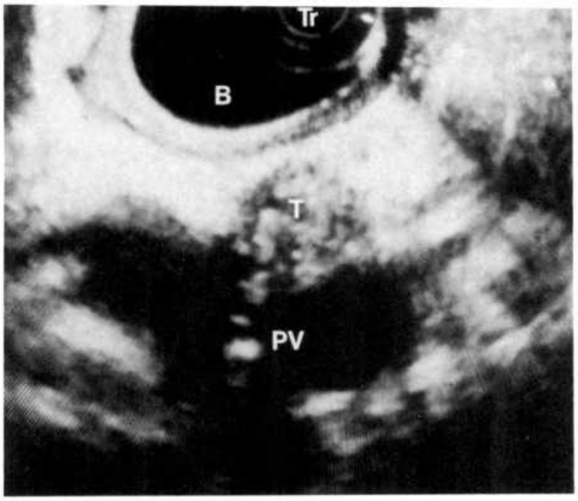

Fig. 6.

Transgastric scan of the porta hepatis (Table III, Case 2). A small tumour (T) less than 1 cm in diameter was visualised obstructing the common hepatic duct. This later proved to be a cholangiocarcinoma. Markers: 1 cm. PV = portal vein, B = balloon around transducer (Tr).

Bile duct

In the two patients with biliary obstruction, a mass lesion (cholangiocarcinoma) was demonstrated in one, and a biliary stricture was not successfully identified in the other.

Discussion

The feasibility of EUS of the upper gastrointestinal tract has been confirmed. Even with the prototype instrument, passage of the endoscope into the oesophagus proved possible in all patients, and from there into the stomach in all patients except for two with oesophageal strictures. When attempted, intubation of the duodenum proved possible in about 75% of cases, as is the experience of Lux et al (1982). The examination normally took from 20 min to half an hour, with a maximum of 45 min. No complications occurred. Scanning failed in six cases, three for technical reasons with the prototype instrument, and three because of difficulties with anatomical orientation.

The prototype instrument has limitations. It is bulky (the rigid tip measures 13 mm in diameter and 45 mm in length), noisy (due to the motor driving the mechanical sector scanner) and rather blunt-ended which makes oesophageal intubation difficult. Problems with the electrical connections between the ultrasound transducer and the shaft of the endoscope occurred after repeated, marked tip deflection required to negotiate the duodenum. The ultrasound sector image was only 180° which meant that, for orientation, repeated electronic rotation of the endoscope (or image) was often necessary. The only system for hard copy was to photograph directly off the monitor, either from the video recording or during the examination. Many of these limitations should be overcome in later generations of equipment. The first commercial instrument, which has just become available (from Olympus Corporation of Japan), has a shorter rigid tip (42 mm), a shaft diameter of 12 mm and displays a full 360° image.

The technique for examination of the upper gastrointestinal tract and contiguous organs by EUS has been described in detail elsewhere (Lux et al, 1982; Strohm & Classen, 1984), but a few points are worth emphasising. The maximum penetration of the ultrasound beam for a useful image is 7–8 cm. A complete survey of the liver, spleen and kidneys is not possible because of the limited penetration of the ultrasound

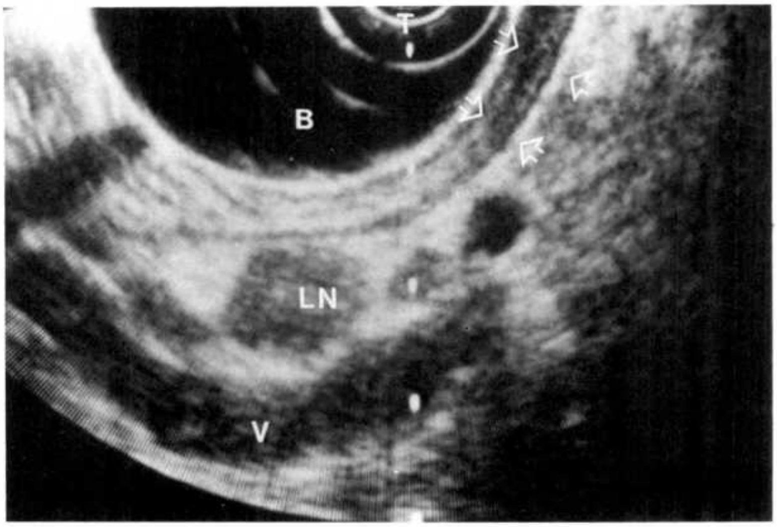

Fig. 7.

Transgastric scan in the region of the coeliac axis in a patient with biochemical evidence of insulinoma (Table III, Case 3). A tumour was seen in the tail of the pancreas and on this and other scans several enlarged lymph nodes were seen around the coeliac axis branches and along the superior border of the pancreas. Diagnosis: metastatic insulinoma. Marker: 1 cm. B = balloon around transducer (T), LN = lymph node, V = vessel, arrowheads = gastric wall.

TABLE IV

PATIENTS WITH SUSPECTED PANCREATIC DISEASE. UNCONFIRMED BUT NEW ABNORMAL FINDINGS DETECTED BY EUS AND CONSIDERED IMPORTANT

Reason for investigation	Previous imaging	Findings on EUS	Follow-up
1 Recurrent pain post-cholecystectomy and sphincterotomy	Routine ultrasound pancreas: normal. Pancreatogram: minimal pancreatitis? Age-related change?	Increased echogenicity around pancreatic duct thought to indicate periductal fibrosis. Lobulated areas of low echogenicity in parenchyma. Diagnosis: chronic pancreatitis	Clinical picture compatible with chronic pancreatitis. Heavy alcohol intake
2 Recurrent abdominal pain	Routine ultrasound and pancreatogram normal	Areas of parenchymal inhomogeneity in pancreas. Pancreatic duct normal. Diagnosis: chronic pancreatitis	Clinical picture compatible with chronic pancreatitis
3 Pancreas divisum	Routine ultrasound and pancreatogram normal	Irregularly lobulated pancreatic outline. Parenchymal irregularity with peripheral areas of low echogenicity. Diagnosis: early chronic pancreatitis	Clinical picture compatible with chronic pancreatitis

TABLE V

PATIENTS WITH KNOWN PANCREATIC DISEASE IN WHOM EUS PROVIDED IMPORTANT NEW INFORMATION, LATER SUBSTANTIATED

Reason for investigation	Previous imaging	Findings on EUS	Confirmation
1 Recurrent pancreatitis	CT and routine ultrasound demonstrated ill-defined mass in body of pancreas. Tumour? Pseudocyst?	Cystic mass in body of pancreas with considerable solid component. Diagnosis: pseudocyst	Surgery
2 Slow recovery in acute pancreatitis	Large pseudocyst and several pseudocysts seen on CT	Only single large pseudocyst detected	Surgery
3 Operability of pancreatic cancer?	Mass in head of pancreas with upstream dilatation of biliary and pancreatic ducts	Mass confirmed, but peripancreatic lymph-node enlargement and micrometastases (1–3 mm) also detected, therefore inoperable (Fig. 8)	2 months later small metastases visible in liver by routine ultrasound. Post-mortem examination confirmed findings 6 months later
4 Obstructive jaundice	Ultrasound indicated dilated bile ducts but no obstructing lesion seen. ERCP: failed cannulation	Head of pancreas mass detected and dilated bile ducts confirmed	Surgery: head of pancreas carcinoma

beam, but the parts of these organs contiguous to the upper gastrointestinal tract are well seen. In the mediastinum excellent views of the heart, in particular the left atrium, left atrial appendage, mitral and aortic valves, and the intra-atrial septum are usually obtained (Hanrath et al, 1983). The technique is not easy. The endoscopy requires familiarity with the use of a side-viewing endoscope, and should be performed only by an experienced endoscopist.

Pancreas

The largest group of patients in this study had proven or suspected pancreatic disease. Important new information was obtained in 11 of the 30 patients scanned for pancreatic indications, and was later independently substantiated in seven. In the four patients with chronic pancreatitis, in whom there was no confirmation of the findings, many of the abnormalities detected were beyond the resolution of other imaging methods available, and only pancreatic biopsy or resection could have substantiated the findings. These included irregular outline of the pancreas, demonstration of lobular inflammation, duct strictures and fibrosis, areas of low echogenicity, increase in periductal echoes, and clubbing of side branches of the main pancreatic duct: all known pathological features of early chronic pancreatitis. There is no doubt that both current imaging tests and biochemical tests are abnormal at only a fairly late stage of chronic pancreatitis. Further studies are

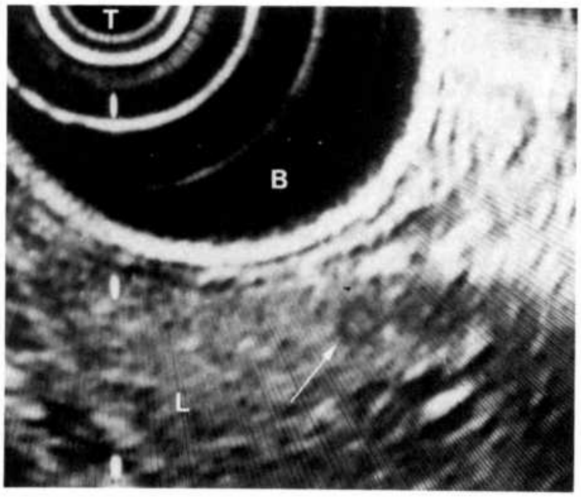

FIG. 8.

Magnified transgastric scan of liver in patient with pancreatic carcinoma (Table V, Case 3). Several small (1–2 mm) target lesions (arrow) were seen studded throughout the liver. Diagnosis: metastases and patient therefore inoperable. Markers: 1 cm. B = balloon around transducer (T), L = liver.

required to test the hypothesis that EUS will provide the earliest diagnosis of this condition.

The differentiation of chronic pancreatitis from carcinoma appears to be more certain by EUS than by conventional ultrasound, but EUS is unlikely to have an important role in the early diagnosis of pancreatic cancer. Most symptomatic patients have relatively advanced disease, easily detected by less invasive imaging modalities, and there is no definable high-risk population for effective screening. However, Yasuda et al (1984), in a series of 15 patients with pancreatic carcinoma, demonstrated that EUS diagnosed two carcinomas under 2 cm not seen by either conventional ultrasound or computed tomography (CT). Endoscopic ultrasound does have great potential as the final filter to screen out patients unsuitable for curative resection, for instance, patients with micrometastases to the liver, as in one of our cases (Fig. 8) and reported by others (DiMagno et al, 1982; Rifkin et al, 1984), or patients with vascular invasion and local lymph-node enlargement.

Another potential role for EUS is in the localisation of pancreatic endocrine tumours. These are normally diagnosed on clinical and biochemical features, but are often too small for accurate localisation by non-invasive means. We localised in the tail of the pancreas an insulinoma that had not been identified on a high-quality CT scan, despite the use of 5 mm sections, bolus enhancement and additional scanning in the right decubitus position. Furthermore, metastatic involvement of the lymph nodes along the coeliac chain was also visualised (Fig. 7), and the findings confirmed at operation. Fukuda et al (1984) reported the successful localisation of an insulinoma by EUS not detected by other imaging methods, including angiography. We also used the same equipment, wrapped in a sterile sheath, to localise intraoperatively a 1 cm insulinoma in the body of the pancreas. Other anecdotal reports of the success of intraoperative small-parts scanners to detect insulinomas suggest that this may prove to be the most accurate and least invasive method (Charboneau et al, 1983; Sigel et al, 1983). However, for pre-operative localisation the high resolution of EUS is unrivalled.

Stomach

Endoscopic ultrasound and intraoperative ultrasound scanning provide unique imaging of the gut wall

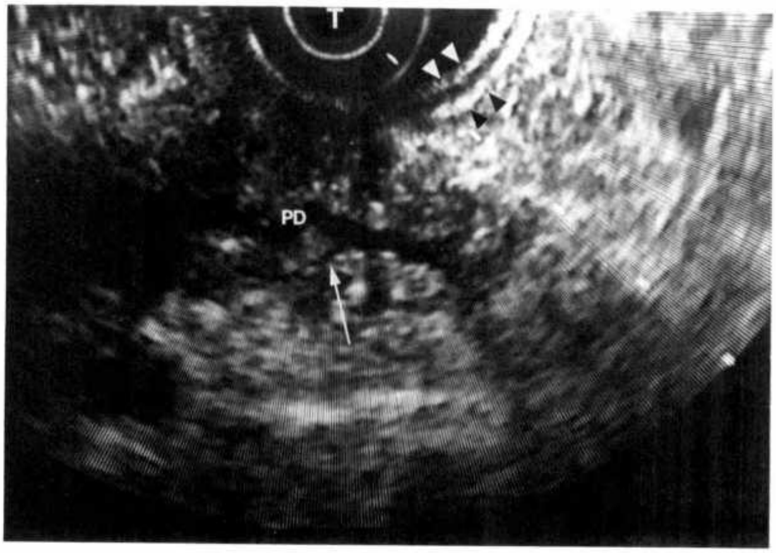

FIG. 9.

Transgastric scan of pancreas. The pancreatic duct (PD) is clearly seen. It is approximately 3 mm in diameter and irregular in outline. Its side branches were also visible and irregular (arrow). The pancreatic texture is inhomogeneous with peripheral areas of reduced echogenicity. The diagnosis was chronic pancreatitis. Markers: 1 cm. T = transducer, arrowheads = stomach wall.

(Caletti et al, 1984; Tio & Tytgat, 1984; Machi et al, 1986). The stomach wall is particularly well demonstrated and resolved into five layers thought to represent the mucosa/stomach lumen interface, the deep part of the mucosa, the submucosa/muscularis mucosa interface, the muscularis propria and the adventitia. Depth of penetration of mucosal lesions is demonstrated by effacement, thickening and destruction of these layers. Local lymph-node enlargement can also be assessed. The technique therefore has the greatest potential of any imaging technique for the most accurate visualisation of local malignant spread.

Oesophagus

The oesophageal wall is differentiated into three layers, two echogenic separated by an echo-poor layer, representing squamous epithelium, muscle and surrounding connective tissue. Our initial experience of imaging oesophageal strictures is encouraging. The depth of spread of intrinsic oesophageal tumours is well demonstrated and may aid in the assessment of operability (Fig. 1). Staging by computed tomography has proved unreliable, because of the inability of CT to resolve the layers of the oesophageal wall and document accurately the extent of mediastinal invasion (Quint et al, 1985). When strictures are due to extrinsic causes the nature of the pathology can often be demonstrated (Figs 2, 3). The major difficulty encountered is in negotiating a tight stricture with the side-viewing endoscope.

Other indications

There do not appear to be many indications for scanning the duodenal wall, although the technique has been shown to be useful for demonstrating the nature of a bulging papilla of Vater to differentiate a tumour from an impacted stone (Tio & Tytgat, 1984).

The role of EUS in hepatobiliary imaging is also likely to be small. Most of the liver lies beyond the range of current equipment, and it is difficult to scan all along the common bile duct because of the limitations of endoscopic movement in the duodenal loop and gastric antrum. However, stones in the common bile duct not visible on conventional external ultrasound examinations have been demonstrated by EUS (Strohm et al, 1984), and in patients with biliary strictures the demonstration of small mass lesions (Fig. 6) can help differentiate malignant from benign disease Micrometastases in the liver beyond the resolution of other imaging modalities may also be detected (Fig. 8).

The cardiac indications are outside the scope of this article but, even in gastroenterological patients, incidental but useful cardiac images may be obtained (Fig. 4).

CONCLUSION

Endoscopic ultrasound is an ingenious marriage of two sophisticated technologies. It is still in its infancy, but already produces high-resolution images of the gut and contiguous organs, providing unique information. With present equipment the procedure is difficult to perform, requiring considerable commitment from both expert ultrasonologist and endoscopist. The number of centres performing this technique is small. This is partly due to the relatively slow development of the prototype instruments, but also because the technique has been adopted largely by endoscopists with little ultrasound training rather than by radiologists, whereas the challenge lies in the difficult ultrasound interpretation rather than the endoscopy. Co-operation between radiologists and endoscopists is essential before the full potential of EUS can be realised. It is unlikely to become a first-line investigation, but with improvements in equipment it should find a useful place in specialist centres, particularly those with interests in pancreatic diseases and gut-wall malignancy, as it can provide clinically useful information not obtainable by any other imaging technique.

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Parathyroid sonography: diagnostic accuracy related to shape, location and texture of the gland

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ABSTRACT

The sonographic features of 51 pathological parathyroid glands detected pre-operatively were analysed. Atypical texture was found in 23.5% and variation in shape in 15.6% of the cases. Cystic parathyroid glands are difficult to differentiate from thyroid cysts, and may be the cause of false positive diagnosis, as in three cases in this series. Topographic assessment showed a relatively low sensitivity in detecting disease in the right upper gland (50%) and in the upper mediastinum (70%). The decreased accuracy in these regions is probably because of the particular anatomical location of the right upper gland and sonographic limitations in screening the mediastinal region. Awareness by the radiologist and surgeon of the variations in texture and location may influence both diagnosis and intraoperative detection of the abnormal parathyroid gland.

Although high-resolution ultrasound has been established as a sensitive and accurate method of parathyroid imaging, there is still difficulty in identifying disease in 8–20% of cases, according to the major reported series (Sample et al, 1978; Duffy et al, 1980; Scheible et al, 1981; Simeone et al, 1981; Reading et al, 1982).

Awareness of different sonographic variations in shape, texture and site of the enlarged parathyroid is essential in the interpretation of results.

PATIENTS AND METHODS

Sonographic examination of the parathyroid glands was performed in 145 patients with hypercalcaemia and clinical suspicion of hyperparathyroidism. Surgical exploration of the neck was performed in 53 patients who form the basis of this study.

Most of the sonograms were performed using a high-resolution dynamic scanner with a 10 MHz transducer (Picker Microview). Four cases were examined with a static grey-scale unit using 5 MHz or 7.5 MHz transducers. The patient was placed in the supine position with the head hyperextended. Longitudinal and transverse sections of the entire thyroid area were performed and the upper mediastinum was routinely scanned by caudal inclination of the transducer. In each case the patient was scanned during swallowing in order to elevate low-lying glands and to assess their mobility. On the basis of the sonographic literature (Duffy et al, 1980; Reading et al, 1982; Stark et al, 1983) and our own experience, the normal parathyroid is generally not visualised sonographically because of its small size and its close anatomic relationship to, and isoechogenicity with, the adjacent thyroid gland. The usual appearance of the enlarged parathyroid gland is generally considered to be anechoic or hypoechoic in texture compared with the thyroid parenchyma, with little or no acoustic enhancement posteriorly. The shape is usually fusiform or oval and the gland is most frequently reported to be localised dorsal to the thyroid gland, separated from it by a thin capsular layer, with cranial mobility on swallowing. The maximum length of the diseased parathyroid glands was measured. Surgical technique included bilateral exploration and exposure of all the glands.

SONOGRAPHIC RESULTS

Location

Fifty-one abnormal glands were located by ultrasound (Table I) with a sensitivity of 82.2%. Eight glands were demonstrated in the posterior mid-portion of the thyroid lobes and could not be ascribed to the upper or lower positions. Of these eight, seven were on the left side (four upper and three lower at operation) and one on the right. The greatest sensitivity was for glands in the left lower position: 100% (22/22), with one false positive error. A high sensitivity rate was also encountered in the left upper (88.8%; 8/9) and the right lower (76.9%; 10/13) positions with a single false positive error per location. Relatively low sensitivity rates were obtained in atypical location (70%; 7/10) and in the right upper position (50%; 4/8).

Shape, pattern and size

In 70.6% of the cases, the sonographic appearance of the enlarged parathyroid gland was typical in both shape and pattern (Fig. 1). In eight enlarged glands out of 51 (15.6%) identified on sonography, the shape of the gland was not oval or fusiform, but assumed

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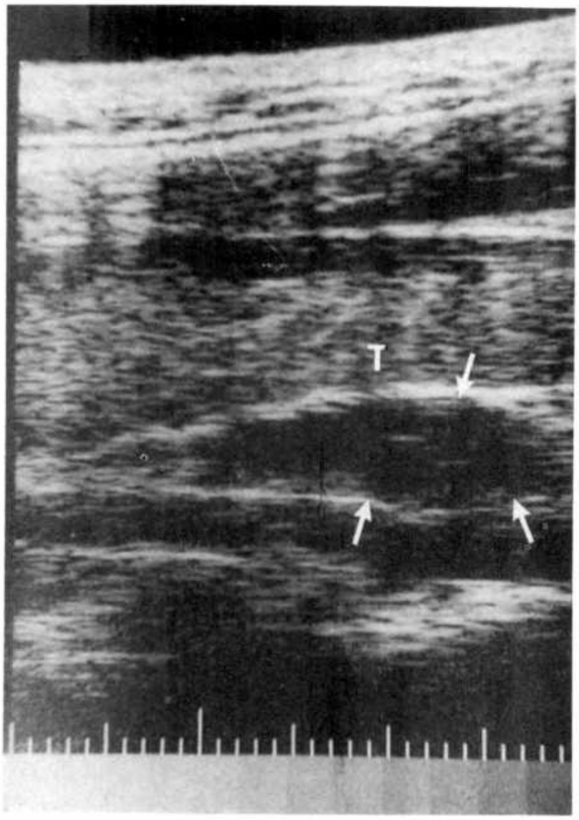

Fig. 1.

Typical sonographic appearance of a parathyroid adenoma in longitudinal section. Note the fusiform, anechoic mass (arrows), separated from the thyroid (T) by a thin echogenic capsule. There is no posterior acoustic enhancement.

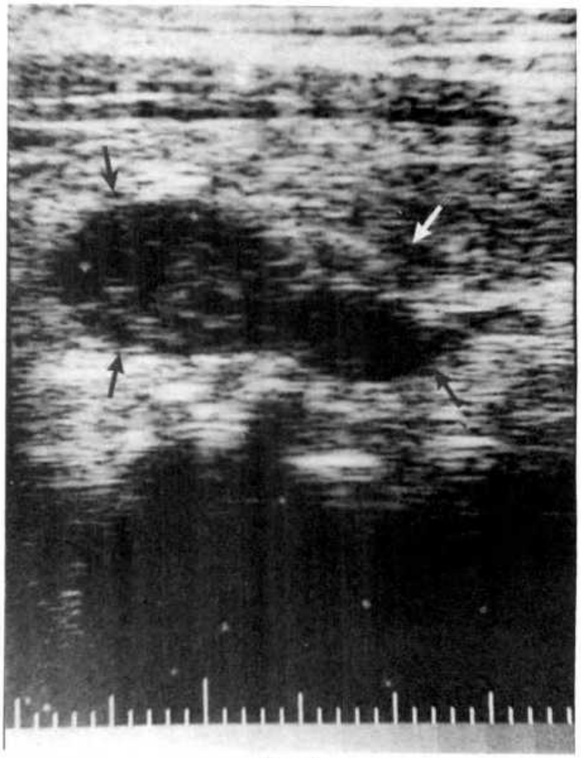

Fig. 2.

Longitudinal scan of the neck showing a bilobular parathyroid adenoma (arrows). Note the presence of echoes within the adenoma.

different configurations, such as teardrop (three cases), irregular (two cases), globular (one case), bilobular (one case: Fig. 2) and kidney-shaped (one case: Fig. 3).

In 12 (23.5%) out of 51 enlarged glands demonstrated, the pattern of the gland was neither purely anechoic nor hypoechoic. Six out of 12 were of mixed type, with both anechoic and echogenic components (Fig. 4). Two of these enlarged glands had cystic components with posterior acoustic enhancement (Fig. 5). Six other glands were isoechoic with the adjacent thyroid gland, from which they could be separated by a thin capsule or halo (Fig. 6).

The mean value of the maximum length of the tumours demonstrated was 16 mm, with a range of 6–35 mm.

Surgical results

Sixty-two abnormal glands were removed at surgery. Of these, 22 (35.4%) were located at the left lower position, 13 (20.9%) at the right lower position, nine (14.5%) at the left upper position and eight (12.9%) at the right upper position (Table I). Ten of the abnormal glands (16.1%) were located in positions considered atypical. Of these, eight were found to be retrosternal

TABLE I

Anatomical distribution of the pathological parathyroid glands at surgery (53 patients) and respective detection accuracy on pre-operative ultrasound assessment

	Right upper	Right lower	Left upper	Left lower	Other localities	Total
Surgical exploration	8	13	9	22	10	62
Ultrasound	4	10	8	22	7	51
Ultrasonic sensitivity (%)	50	76.9	88.8	100	70	82.2

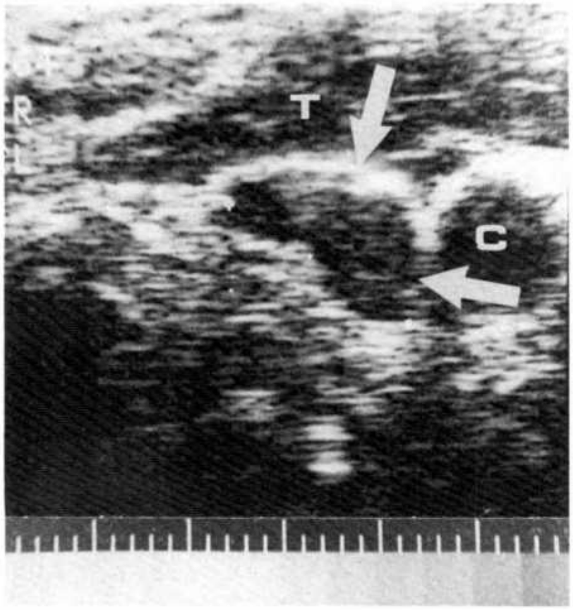

FIG. 3.

"Kidney-shaped" adenoma of the parathyroid gland (arrows), with moderate internal echogenicity. Transverse section; T = thyroid, C = common carotid artery.

and two were located within the thyroid tissue. The largest parathyroid tumour missed on sonography in our series measured 45 mm in its longest axis, and was located in the mediastinum at surgery. The smallest undetected tumour measured 10 mm.

Persistent post-operative hypercalcaemia was encountered in two patients. In one, a mediastinal gland was removed on re-exploration. In the second patient, two enlarged glands were removed at surgery, leaving intact two glands which appeared normal. Pathological assessment of the glands removed revealed hyperplasia.

Diagnostic accuracy

The diagnostic sensitivity of sonography in the detection of pathological parathyroid glands in this series is 82.2%. In order to obtain an estimate of specificity, each patient was considered to have four

TABLE II

DIAGNOSTIC ACCURACY OF ULTRASOUND IN THE EXAMINATION OF 212 PARATHYROID GLANDS

	Surgical exploration positive	Surgical exploration negative
Ultrasound positive	51	3
Ultrasound negative	11	150

Sensitivity = 82.2%; specificity = 98%; predictive value of positive test = 94.4%; predictive value of negative test = 93.1%; accuracy = 93.4%.

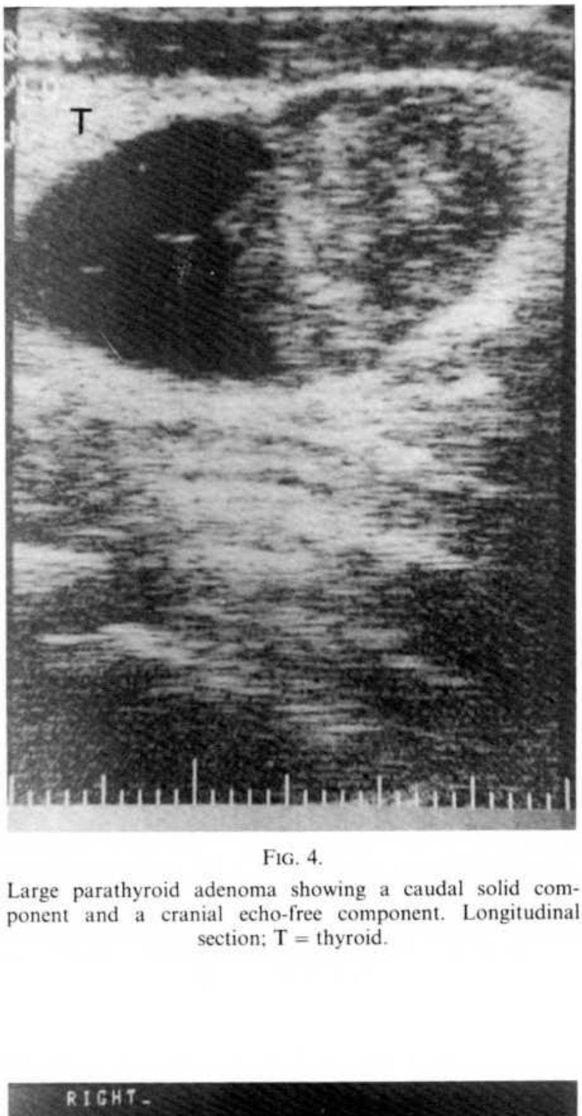

FIG. 4.

Large parathyroid adenoma showing a caudal solid component and a cranial echo-free component. Longitudinal section; T = thyroid.

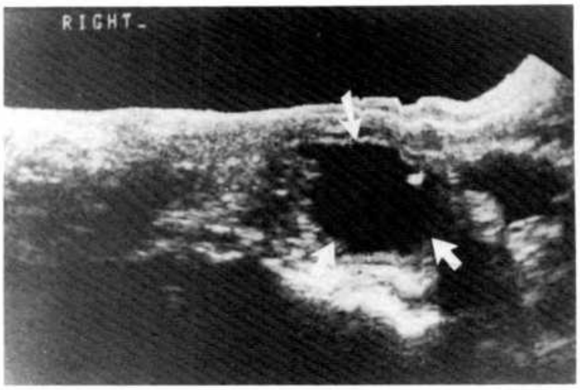

FIG. 5.

Longitudinal scan of the right neck showing a cystic parathyroid gland (arrows) with increased posterior enhancement.

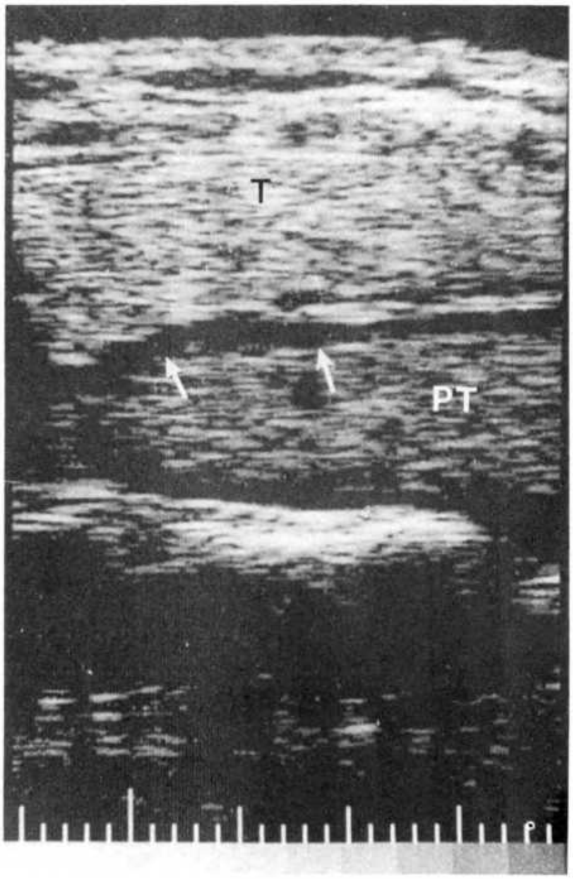

FIG. 6.

Large parathyroid adenoma (PT) almost isoechogenic with the thyroid (T), from which it is separated by a thin echogenic layer and an echo-free halo (arrows). Longitudinal section.

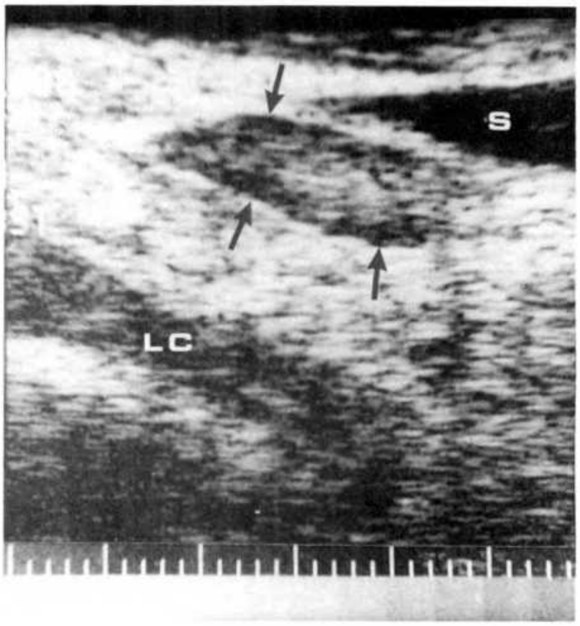

FIG. 7.

Longitudinal scan during swallowing showing an enlarged parathyroid gland (arrows) in the upper mediastinum surrounded by fat. Thyroid parenchyma is not seen. The longus colli muscle (LC) is seen posterior to the enlarged gland, and the sternocleidomastoid muscle (S) ventro-caudal to the gland.

parathyroid glands, and each was analysed separately (Table II).

The 53 patients were considered to have 212 glands. Of these, 62 were found to be abnormal at the time of operation and the other 150 were assumed to be normal. There were three false positive studies which, at surgery, proved to be posteriorly protruding thyroid colloid cysts. The mean value of the maximum length of the false negative glands (19 mm) did not differ significantly from the mean length of the true positive glands (16 mm). The results show a specificity of 98%, a predictive value of a positive test of 94.4% and an overall accuracy of 93.4%.

DISCUSSION

High-resolution sonography is a reliable method for imaging pathological parathyroid glands, with a reported accuracy ranging from 65% to 92%. The enlarged gland is classically described as being anechoic or hypoechoic relative to the adjacent thyroid parenchyma, with little or no posterior acoustic enhancement. The parathyroid tumour is usually oval or fusiform in shape, and located posterior to the thyroid, from which it is separated by a thin capsule (Fig. 1) (Sample et al, 1978; Duffy et al, 1980; Scheible et al, 1981; Simeone et al, 1981; Reading et al, 1982; Stark et al, 1983). Two reports have discussed variations in sonographic shape and texture of the enlarged parathyroid glands. One report described a spectrum of parathyroid tumour echogenicity from cystic to solid (Simeone et al, 1981) and cystic parathyroid tumours are reported on sonography by Krudy et al (1984).

Analysis of the sonographic features in 51 pathological glands detected by ultrasound revealed an atypical texture in 23.5% (12/51) and non-classical shape in 15.6% (8/51). Variations in shape and size did not affect the level of confidence in identifying the enlarged glands since similar configurations have been well documented previously (Wang, 1976; Akerstrom et al, 1984). However, variations in texture may present diagnostic difficulty. While isoechogenic pathological glands can usually be differentiated from adjacent thyroid tissue by a separating capsule, it may be more difficult to distinguish cystic glands from thyroid cysts. In fact, all three false positive cases in this series proved at surgery to be protruding thyroid cysts. Similar difficulty in differentiating hyperfunctioning cystic parathyroid glands from incidental thyroid cysts was experienced by Krudy et al (1984), who suggested fine-needle aspiration biopsy and assay of parathyroid hormone.

Evaluation of the surgical findings showed that most of the undetected pathological glands were situated in the right upper position in relation to the thyroid, and in the mediastinum. The relatively low accuracy in the mediastinum is not surprising considering the limitations of sonography in the chest, although cranial migration during swallowing may be helpful in some cases (Fig. 7). The use of 10 MHz transducers with a smaller scan head may permit an easier approach to mediastinal glands. The reason for the relative difficulty encountered in the detection of the right upper gland is not clear. A partial explanation can be suggested by Wang's observation in autopsies (Wang, 1976), where 77% of the upper glands were located at the postero-lateral aspect of the cricothyroid junction, while only 22% of the glands were situated at the posterior aspect of the upper thyroid pole. The cartilaginous structures of the larynx may, therefore, render the upper glands less accessible to the ultrasound beam. Since Akerstrom et al (1984) pointed out, in an autopsy study, that the glands are usually symmetrical, we have no explanation for the difference in our sonographic sensitivity between the left and right side of the neck.

In general, this series indicates that adenomas of the parathyroid gland are demonstrated with a greater degree of accuracy on the left side (94.4%) than on the right (63.4%), and the lower glands identified more accurately than the respective upper glands. In cases where patients undergo surgery despite a negative ultrasound study, the exploration is likely to be more fruitful on the right side of the neck, and more specifically in the region of the right upper gland. A supernumerary gland in the thymus must also be excluded.

ACKNOWLEDGMENT

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Book review

Ultrasound-guided Biopsy and Drainage. By Rainer Ch Otto and J. Wellauer, pp. xi+160, 1986 (Springer Verlag, Berlin), DM78.
ISBN 3-540-16241-0 (Berlin)
0-387-16241-0 (New York)

Biopsy procedures performed under imaging guidance are preferred to blind biopsies because of the improved accuracy and safety when the needle is visualised in relation to the target and potentially sensitive structures that should be avoided Ultrasound is perhaps the simplest guidance technique because of its immediacy and its real-time display. This book discusses the applications of ultrasound to biopsies, both cytological and histological, and for therapeutic drainage procedures. The authors' experience in ultrasound-guided biopsies well qualifies them for this task; they have developed several special needles which have become widely accepted, especially the fine-cutting "Zurich" needle, which here receives due mention

Biopsy techniques are described in the first main section with discussion of ease of visualisation of various types of needle A second main section details methods of preparation and handling of specimens, and covers the diagnostic accuracy obtained site by site. An evaluation of the risks confirms the consensus that fine-needle procedures employed with circumspection are very safe and usually are the least hazardous method of obtaining histological samples. The last section returns to two of the main areas of application, the liver and kidneys, with further practical points before moving on to drainage procedures for the kidney and pancreas. This rather arbitrary arrangement of the sections results in some duplication and unnecessary separation of material that refers to one subject. A few useful applications are not mentioned, *e.g* chest, pericardial and ascites drainage. Throughout the text the authors' own guidance technique using a centre notched linear array is stressed, many potential users of ultrasound for guidance will not want to invest in such a specialised transducer, especially since it produces degraded images, and would find the free-hand technique or the use of a detachable needle guide with either sector or linear transducers more readily available and equally useful In addition, the automatic biopsy gun (Biopty) is not mentioned, no doubt because it is a recent introduction Since the gun simplifies and speeds the procedure, it is likely to find general acceptance.

Notwithstanding these minor reservations, this little book is a very useful and practical guide to the uses and limitations of ultrasound-directed biopsies. The importance of this technique recommends this book to all ultrasound users.

David O. Cosgrove

1987, *The British Journal of Radiology*, 60, 445–447 MAY 1987

Dehydration, antidiuretic hormone and the intravenous urogram

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ABSTRACT

The efficacy and safety of attempts to dehydrate patients before intravenous urography in order to improve image quality have been called into question by several authors. Antidiuretic hormone (ADH) assays described here show that dehydration of outpatients as typically practised by radiology departments does not affect plasma ADH levels. Furthermore, the very act of contrast-agent administration causes a rapid rise in plasma ADH concentration to levels higher than would in any case be expected from modest dehydration. Since the likely effect on circulating ADH of attempted dehydration is dwarfed by the physiological response to a contrast agent, it is considered that such efforts are entirely superfluous.

A regime of dehydration for some hours before intravenous urography is a traditional part of patient preparation for the procedure (Saxton, 1969). The theoretical basis for it is that the elevated levels of antidiuretic hormone (ADH) produced as a result will enhance the reabsorbtion of water from the distal and collecting tubules of the kidney, thereby concentrating urinary contrast agent to produce a radiographically denser, though perhaps less well distended, pyelogram.

Cattell et al (1967) showed that in the dehydrated state, urine concentrations of sodium diatrizoate (Hypaque, Winthrop) could be four times those after hydration, though, as pointed out by Saxton (1969), the degrees of both hydration and dehydration were more marked than is likely in everyday clinical practice.

Benness (1967) showed that fluid deprivation for 2–3 days produced an increase in the urinary concentration of contrast agent, but again, this degree of dehydration is not routinely achieved.

More recent work by Bell and McIlrath (1985) has demonstrated that the more modest dehydration that is generally achieved before intravenous urography was not successful in improving any aspect of diagnostic image quality. Furthermore, current understanding of contrast agent related renal function impairment suggests that more effective regimes of dehydration may be dangerous, particularly in diabetics and the elderly (Webb et al, 1981, Dawson, 1985).

Since plasma osmolality and blood ADH levels provide an index of the degree of dehydration, we have monitored both in some routinely dehydrated patients who were undergoing intravenous urography, in order to test the effectiveness of dehydration in producing the theoretically required rise in ADH concentration.

PATIENTS AND METHODS

Patients were taken from the routine workload of intravenous urography at two hospitals and were unaware that they would be included in the study before they entered the X-ray room. All had been instructed to take nothing orally after their evening meal, the evening before the examination, and had thus been dehydrated for between 9 h and 18 h, depending on the time of the examination. Patients with any known renal, cardiac or alcohol-related diseases were excluded, as were those taking thiazides, lithium, tetracyclines and chlorpropamide, as they are all said to influence ADH concentrations and responses.

Six patients received 60 ml sodium iothalamate (Conray 420, May & Baker) (42 g) and six patients received 50 ml sodium meglumine diatrizoate (Urografin 325, Schering Ltd) (meglumine diatrizoate, 9 g; sodium diatrizoate, 20 g). Blood samples were taken for determination of osmolality and ADH concentrations before rapid bolus administration of contrast agent and at 2 min and 20 min after. These times were chosen because studies of the release and metabolism of ADH suggest that these times should coincide with a peak concentration and a concentration about four half-lives after the initial contrast-agent stimulus (Fabian et al, 1969). The initial samples were taken after the patients had been seated for about 15 min.

A record was kept of any side-effects perceived by patients to be due to contrast agents, and these were scored according to their severity in order to exclude, for example, excessive nausea as a cause of a transient rise in ADH levels.

Blood samples were immediately chilled to 4°C and were spun down in a refrigerated centrifuge within 45 min of being taken. After centrifugation at 2000 rpm for 5 min at 4°C, the plasma was separated until analysis of plasma ADH, which was performed by radioimmunoassay as described by Aziz et al (1981). The plasma was extracted using bentonite (Skowsky et al, 1977) and iodinated ADH prepared using the solid-phase lactoperoxidase method (Karonen et al,

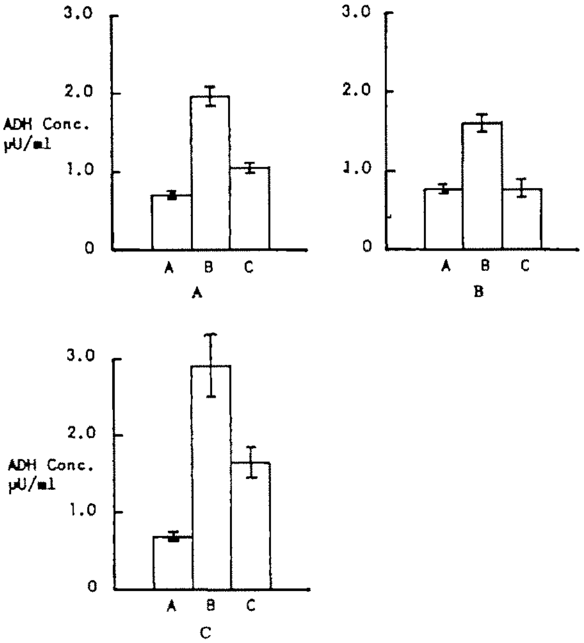

Fig. 1.

Graphs showing antidiuretic hormone response to administration of intravenous contrast agents. A, ADH concentration before injection of contrast agent, B, ADH concentration after 2 min, C, ADH concentration after 20 min. (A) Combined data, (B) Urografin 325, (C) Conray 420

1975). Where possible, samples were assayed together in the same run to minimise interassay variation. The inter- and intra-assay variation coefficients for ADH were 11.9% and 7.7%, respectively. Circulating contrast agents do not appear to interfere with the assay method.

Osmolality determinations were by the freezing-point depression method

Results

Figure 1 shows plots in histogram form of the mean ADH concentrations at the three sampling times, with standard errors and mean indicated, both for the two different contrast-agent groups separately and for all samples taken together.

The normal range of ADH concentrations in healthy individuals is 0.4–1.5 μU/ml. The mean level of ADH before contrast-agent injection lies within this range, but following the injection there is a rapid and marked rise in ADH, the levels declining over the succeeding 20 min. The rises are significant and greater in the Conray group of patients ($p < 0.05$) and less in the Urografin group ($p < 0.05$)

The plasma osmolality measurements showed no significant change after the injection. The mean osmolality before injection of contrast agent was 289 mosmol/l (SD = 2.8), at 2 min after the injection was 291 mosmol/l (SD = 3.3), and at 20 min was 290 mosmol/l (SD = 2.6). The normal range of serum osmolality is 280–300 mosmol/l.

Discussion

The fact that all the supposedly dehydrated patients had ADH concentrations within the normal range demonstrates the complete ineffectiveness of attempts at dehydration as typically practised at two hospitals. More surprising is the precipitate rise in circulating ADH concentrations within 2 min of the injection of contrast agent. The lack of a corresponding measurable change of serum osmolality after the injection presumably reflects dilution of the hyperosmolar medium and its rapid renal excretion. The serum osmolality is thereby normalised by 2 min after the injection.

There are several mechanisms which could explain the modulated ADH levels recorded during intravenous urography:

(a) a response to the "stress" of the procedure,
(b) a response to the osmotic load of the contrast agent, and
(c) a response to the administered volume load

(a) Stress

Stress and nausea are among the factors known to cause rises in blood ADH concentrations (Rowe et al, 1979; Forsling et al, 1984) The extent to which such factors may have influenced our results is difficult to estimate. Contrast agents are, of course associated with a variety of disturbing subjective side-effects. No correlation was found between ADH response and patients' subjective side-effects as revealed by direct questioning. It is likely that patients experience stress at intravenous urography, but animal studies suggest that only the more severe types of stressful stimuli are likely to cause ADH levels to rise to the degree seen here.

No data are available on ADH release in man during stress, except during surgery.

(b) Osmotic load

A response to the osmotic load presented by the contrast agent seems a likely explanation of the observed results. The osmolalities of the contrast agents were 2496 mosmol/kg for Conray 420 and 1650 mosmol/kg for Urografin 325 The total osmotic loads were, therefore, greater with Conray than with Urografin. If the ADH response is mediated by osmolality, ADH with its half-life of about 5 min presumably acts as a persisting marker of the initial hyperosmolality surge following contrast-agent injection which is perceived at key sites. As would be expected, if this phenomenon is driven by osmolality, the response to the smaller total osmolar load given in the Urografin group of patients is significantly less ($p < 0.05$) than in the Conray group. No data are available on the time course of change in plasma osmolality following administration of a hyperosmolar bolus in man.

(c) Volume load

Another factor deserving consideration is the impact of a sudden volume load on the circulation, and particularly on the right atrial stretch receptors. Animal studies (Abed et al, 1982) have shown that stimulation of atrial stretch receptors can produce a fall in blood ADH levels as well as other hormonal responses. If these data are extrapolated to man, osmotic and volume-load effects oppose. From unpublished animal studies (Forsling, unpublished data), it is known that following a peripheral venous volume load of the magnitude relative to body size being considered here, little atrial ADH response is seen. It therefore seems probable that the osmotic response predominates in this clinical context. However, in the case of rapid delivery of a bolus of contrast agent directly into the right atrium, as in digital subtraction angiography, the opposing osmotic and volume-based effects are both likely to be contributory and a study is under way to evaluate their relative contributions.

Whatever the fundamental mechanisms involved, our results show that the injection of contrast agent produces circulating ADH concentrations at least as high as could be hoped for from effective dehydration. These concentrations are reached very soon after injection and prevail well before the time that the pyelography is performed. They are likely to have a significant effect on the kidney because the dose–response curve of ADH in producing antidiuresis is steep, and maximal antidiuretic response in man is achieved at about 5–10 μU/ml (Martin et al, 1975; Fieldman et al, 1985).

With this in mind, and because routinely attempted dehydration appears to be ineffective in practice and possibly dangerous, we suggest it should now be abandoned.

ACKNOWLEDGMENT

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Book review

Comprehensive Care for Craniofacial Deformities. Ed by Jeffrey L. March and Michael W. Vannier, pp xxv+323, 1985 (Blackwell Scientific Publications, Oxford), £68 00
ISBN 0–8016–3167–X

This is a multiauthor text from the craniofacial team at the Cleft Palate & Craniofacial Deformities Institute which is part of the Washington University Medical Center, St Louis, Missouri. It documents experience gained since 1978 in evaluating and providing care for 1013 patients with cleft lip and/or palate and other craniofacial deformities. The book is divided into two sections: general concepts and clinical management.

The first section describes in some detail the craniofacial team and the role of each member in the context of a multidisciplinary approach. This section also includes chapters on genetics, radiological assessment, anaesthetic concerns and associated medical, neurological and psychological problems. The chapter on radiological assessment highlights the expertise of Dr Vannier and his team It covers routine radiological techniques including cephalometry, standard axial computed tomography scans and the more advanced technology of reformatted images and three-dimensional surface reconstruction. Brief reference is made to nuclear magnetic resonance scans, but the three-dimensional technique is still in the process of development, and its role in the assessment of craniofacial deformities is yet to be defined.

The second section deals with the evaluation and clinical management of a variety of craniofacial deformities arranged according to the major anatomical areas: calvarium, orbit, midface, unilateral major facial, bilateral major facial, ear and cleft lip and palate. The chapter describing the normal development and growth of the head utilises a series of skulls and osseous reconstructions to demonstrate various points In the other chapters, specific cases are used to illustrate each anatomical area with the extensive use of visual presentation by means of clinical photographs, radiographs and computed tomography images with three-dimensional and coronal reconstructions The abnormal is compared with the normal and the pre-operative is compared with the post-operative. Unfortunately, the pre- and post-operative photographs, radiographs and osseous reconstructions are frequently on different pages, thus presenting some difficulty when the reader attempts to evaluate the results of surgery.

Despite this criticism, the book provides an excellent overview of the assessment and care of patients with craniofacial anomalies, and the pitfall of too much surgical detail has been avoided. Undoubtedly this book will be read with considerable interest by surgeons involved in the care of such patients, and they are likely to be requesting their radiological colleagues to provide some of the more advanced imaging techniques described in it. The quality of production is high, and the book is an essential volume in the library of any department interested in the field of craniofacial deformity.

D. R. JAMES

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Subepithelial pyeloureteric lesions in patients with nephrostomy tubes

By D. A. Cory, M.D., R. D. Tarver, M.D., M. K. Baker, M.D., J. L. Wass, M.D., *R. C. Rink, M.D. and *M. E. Mitchell, M.D.

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(*Received August 1986*)

ABSTRACT

Mural filling defects were identified in the renal pelves or ureters in five patients with nephrostomy tubes. In two patients, infection was documented. In the remaining patients, the urine was sterile. While typical ureteritis cystica associated with infection may be seen in patients with nephrostomy tubes, in some patients, other mechanisms are responsible for this appearance.

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Ureteritis cystica is a condition of multiple fluid-filled cysts in the submucosa of the ureter which occur in the presence of persistent or recurrent infection. Similar changes may occur in the renal pelvis (pyelitis cystica) or bladder (cystitis cystica) (Elkin, 1980). The urographic appearance of these entities may be mimicked by several other conditions including subepithelial haemorrhage (Thompson & McAlister, 1975) and oedema (Levine et al, 1982). We have identified mural filling defects with an appearance like pyelitis or ureteritis cystica in five patients with nephrostomy

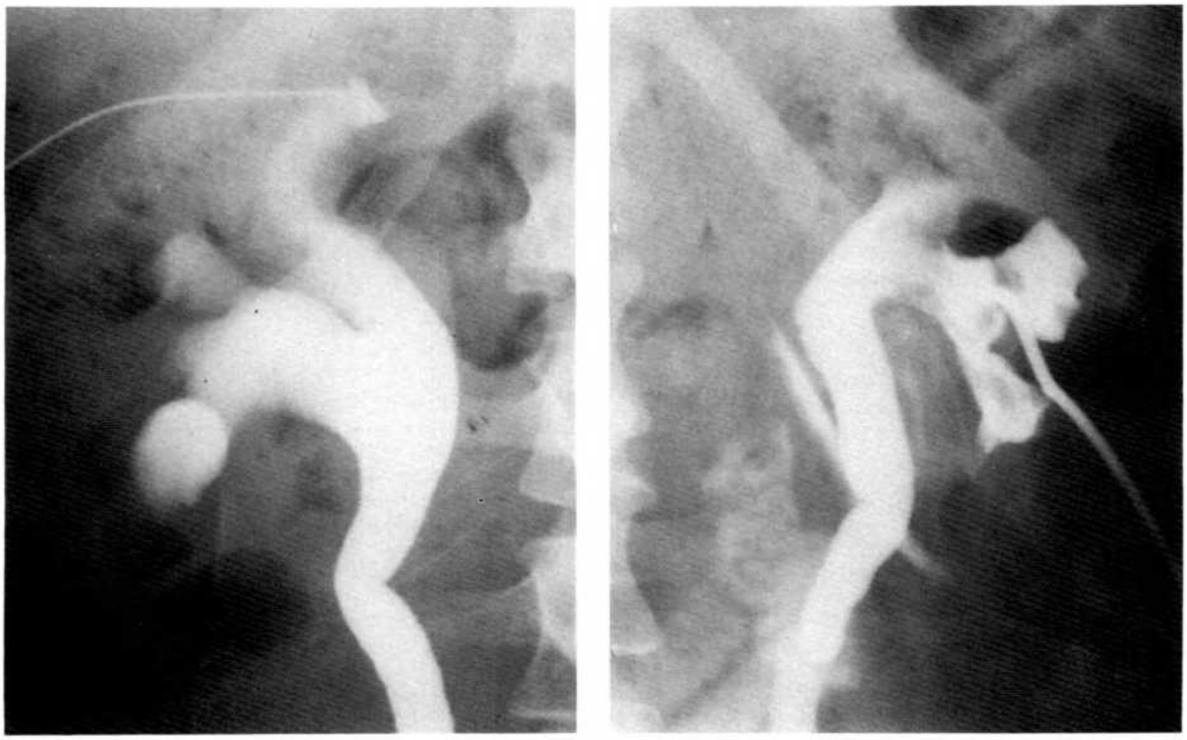

FIG. 1. *Case 1.*

(A) Right antegrade pyelogram prior to nephrostomy-tube placement shows smooth contour of the collecting system. (B) Left nephrostogram immediately after tube placement shows smooth contour of the collecting system.

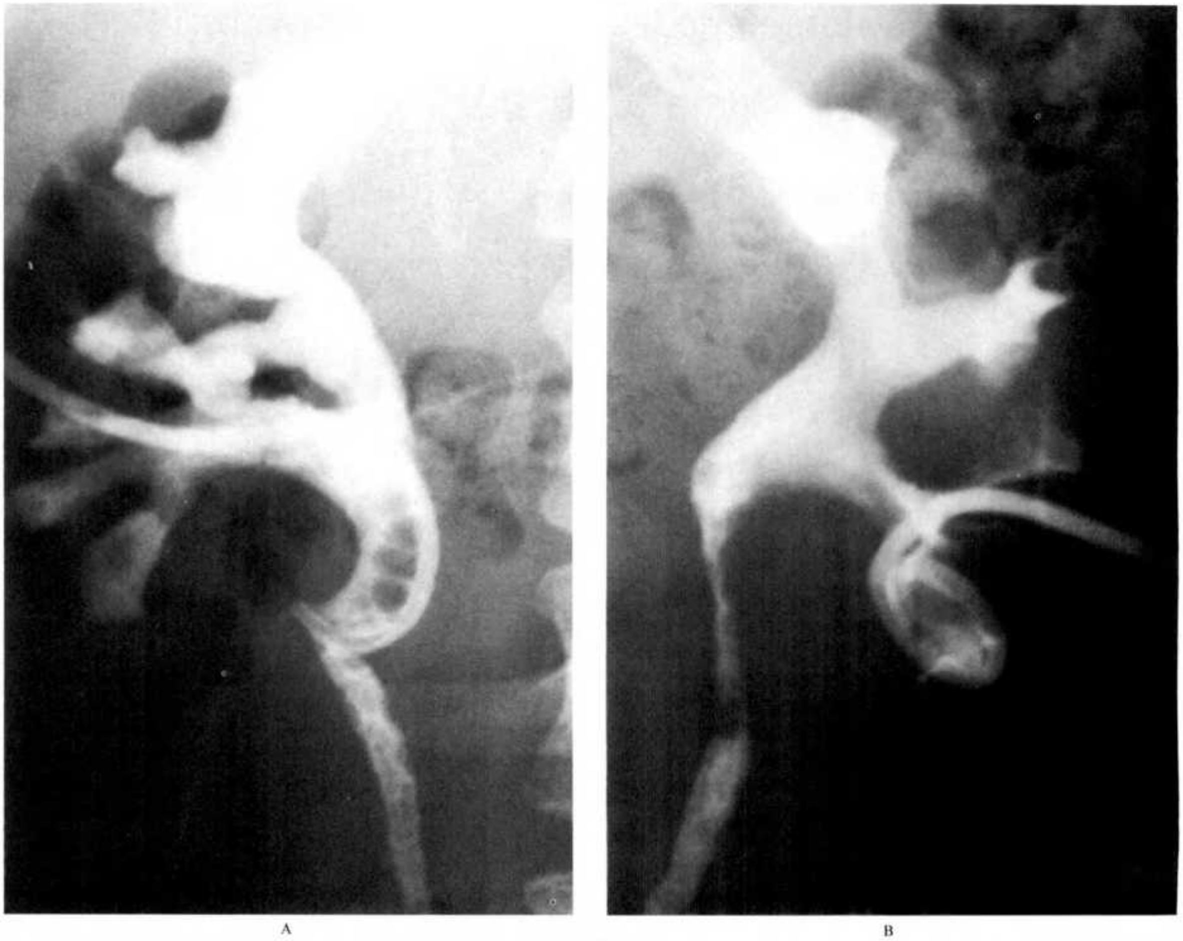

Fig. 2. *Case 1.*

(a) Right nephrostogram 2.5 weeks later shows pigtail catheter in the renal pelvis with nodular filling defects extending distally in the ureter. (b) Left nephrostogram shows filling defects in the ureter remote from the pigtail catheter which lies in a lower-pole calyx.

tubes. Infection is likely to have played a role in two cases, but in the other three cases cultures were negative. In the non-infected patients, reaction of the uroepithelium to the nephrostomy tube must be implicated in producing the radiographic changes.

Case Reports

Case 1

A 20-year-old white man developed bilateral hydronephrosis secondary to ureteric obstruction by disseminated, undifferentiated carcinoma. Bilateral nephrostomy tubes were placed percutaneously. Antegrade pyelograms at the time of tube placement (Fig. 1) showed bilateral hydronephrosis only. Urine cultures were negative. Follow-up nephrostograms approximately 2.5 weeks after tube placement showed multiple nodular filling defects in the walls of both ureters (Fig. 2). The urine remained sterile.

Case 2

A 4-year-old white boy with bilateral vesicoureteric reflux underwent bilateral ureterovesical re-implants. A pre-operative urine culture was negative. Post-operatively, the patient was oliguric and became hyperkalaemic due to bilateral ureterovesical junction obstruction. A left nephrostomy tube was placed on the second post-operative day, with subsequent good urine output through the tube and correction of electrolyte imbalance. On the eighth post-operative day, intravenous pyelography (IVP) showed persistent obstruction on the right, and a right percutaneous nephrostomy tube was placed. Right nephrostography performed 5 days after placement showed the tube looped in the pelvis, and mural nodular filling defects adjacent to the tube (Fig. 3). Another nephrostogram 4 days later showed the tube to have moved slightly and resolution of the filling defects (Fig. 4).

Case 3

A 4-year-old white boy with myelomeningocoele and vesicoureteric reflux underwent bilateral ureterovesical re-

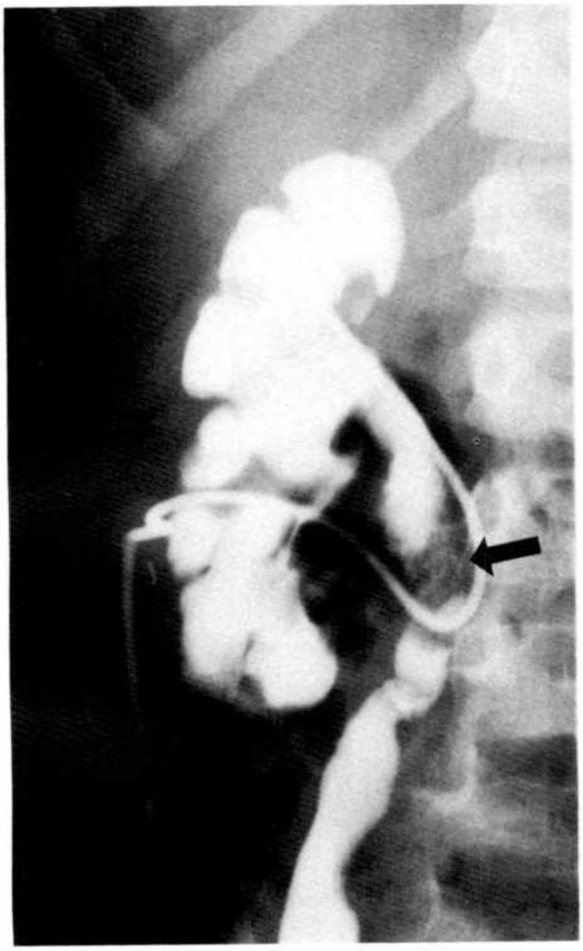

FIG. 3. *Case 2.*

Nephrostogram shows small nodular filling defects (arrow) in the renal pelvis adjacent to the nephrostomy tube.

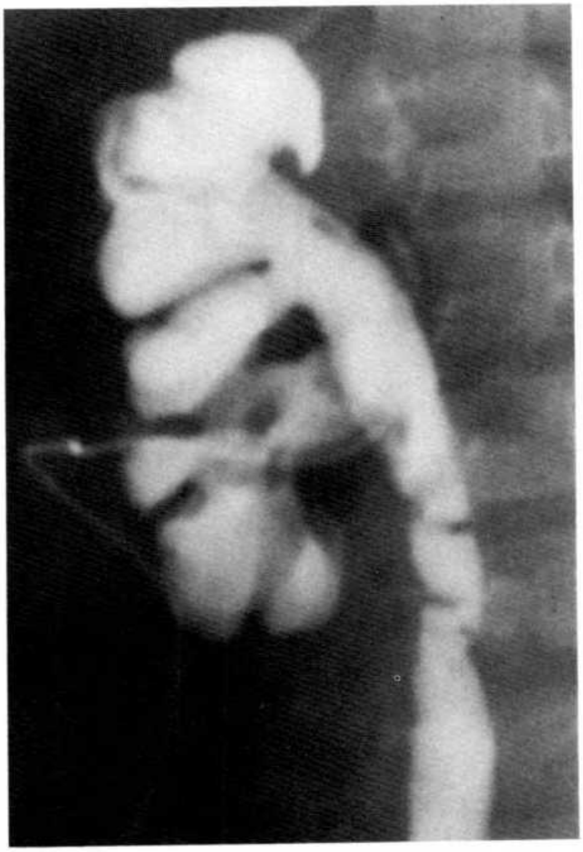

FIG. 4. *Case 2.*

Nephrostogram after movement of the tube shows that the filling defects have resolved.

implants with placement of 5-French ureteric stents. The patient had a history of urinary tract infections, but had been free of infection for 1.5 years on antibiotic suppression. Urine cultures 1 day pre- and post-operatively were sterile.

Following removal of the ureteric stents, the patient had reduced urine output and a $^{99}Tc^{m}$ DTPA renal scan showed non-function of the right kidney. A nephrostomy tube was placed and an antegrade pyelogram showed the ureter to have a smooth contour (Fig. 5). A nephrostogram 1 week later showed multiple nodular filling defects in the ureteric wall (Fig. 6). Cultures of urine from the nephrostomy tube were negative.

Case 4

A 45-year-old white man with a history of bilateral renal calculi and urinary tract infections underwent a right pyelolithotomy and nephrostomy. Tomograms 6 weeks later showed a left staghorn calculus and a retained stone on the right. A right nephrostogram showed changes of ureteritis cystica. The patient was admitted for left nephrolithotomy. Urine cultures on admission were positive for *Klebsiella* and *Staphylococcus*. Treatment with tobramycin was initiated and left nephrolithotomy and nephrostomy were performed. A nephrostogram 11 days post-operatively showed filling defects in the wall of the left ureter (Fig. 7A). Cultures from the left nephrostomy were positive at the time of the nephrostogram.

Case 5

A 63-year-old black woman with a history of bilateral ureteric calculi and chronic urinary tract infections developed bilateral staghorn calculi. She underwent nephrolithotomy on the right, with a nephrostomy tube left in place post-operatively. *Providentia stuartii* was cultured from the staghorn calculus. Nephrostography 9 days post-operatively revealed multiple filling defects in the ureteric wall (Fig. 7B). Urine culture grew three gram-negative organisms at that time.

DISCUSSION

The walls of the renal pelvis and ureter are composed of three layers: mucosa, muscularis and adventitia. The

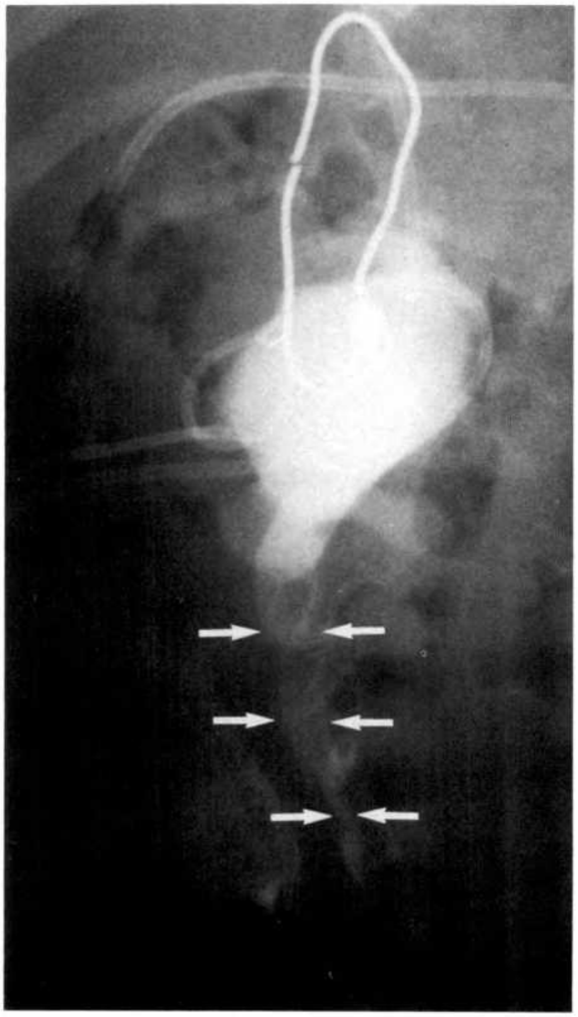

Fig. 5. *Case 3.*

Injection of contrast medium immediately after nephrostomy-tube placement shows smooth contour of the ureter (arrows). A ventriculo-peritoneal shunt catheter and a wire from prior spinal fusion are superimposed on the renal pelvis.

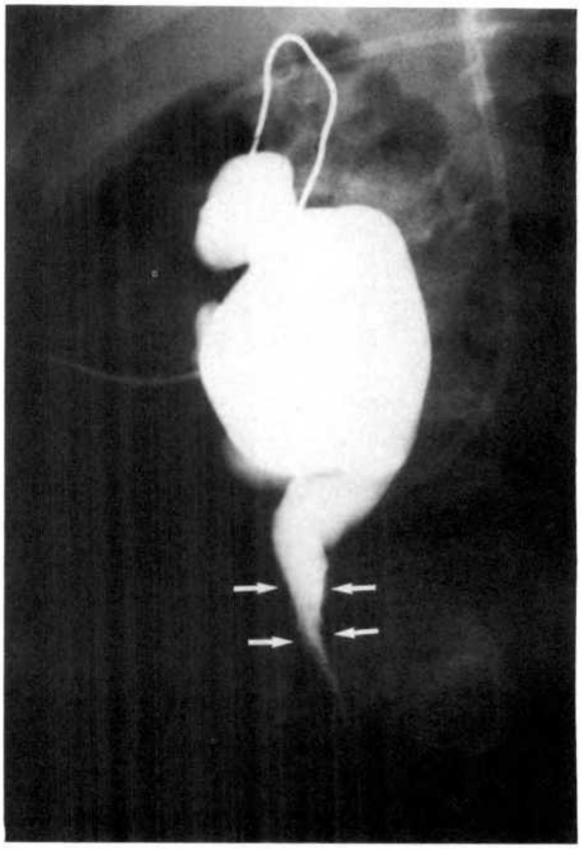

Fig. 6. *Case 3.*

There are nodular filling defects (arrows) in the ureter on a follow-up nephrostogram 1 week after placement of the tube.

mucosa consists of a layer of transitional epithelium and the lamina propria, a connective-tissue layer which loosely attaches the epithelium to the muscularis (Bergman, 1981). In pyeloureteritis cystica, fluid-filled cysts lined by transitional epithelium are found in the lamina propria impinging on the lumen. The mechanism of formation of these cysts is unknown, but may be due to downward proliferation of epithelial cells in response to chronic infection (Elkin, 1980). In our Cases 4 and 5, there was a history of chronic urinary tract infection, with positive cultures during the period the nephrostomy tubes were in place. The radiographic changes in these cases were probably related more to infection than to the presence of the tubes.

Subepithelial oedema may mimic pyeloureteritis or cystitis cystica. Direct irritation of the renal pelvis by nephrostomy tubes (Harris et al, 1976) or the bladder by indwelling catheters (Elkin, 1980) produces bullous oedema. Oedema secondary to ureteric stents, with or without infection, may be severe enough to cause obstruction after stent removal. Direct irritation explains the findings in Case 2, where nodular changes in the pelvis appeared and resolved quickly, in association with movement of the tube. In the remaining two cases, the filling defects were seen in the ureter, distal to the nephrostomy tubes. The urine was not infected in these patients. There are two possible explanations for these changes in the ureter. First, oedema incited by direct contact of the catheter with the ureteric mucosa may spread distally in the loose connective tissue of the lamina propria. Such an occurrence could explain the appearance of the ureter on the right in Case 1 (Fig. 2A), where the filling detects extend distally from the level of the tube. However, in the same patient (Fig. 2B), the filling defects on the left

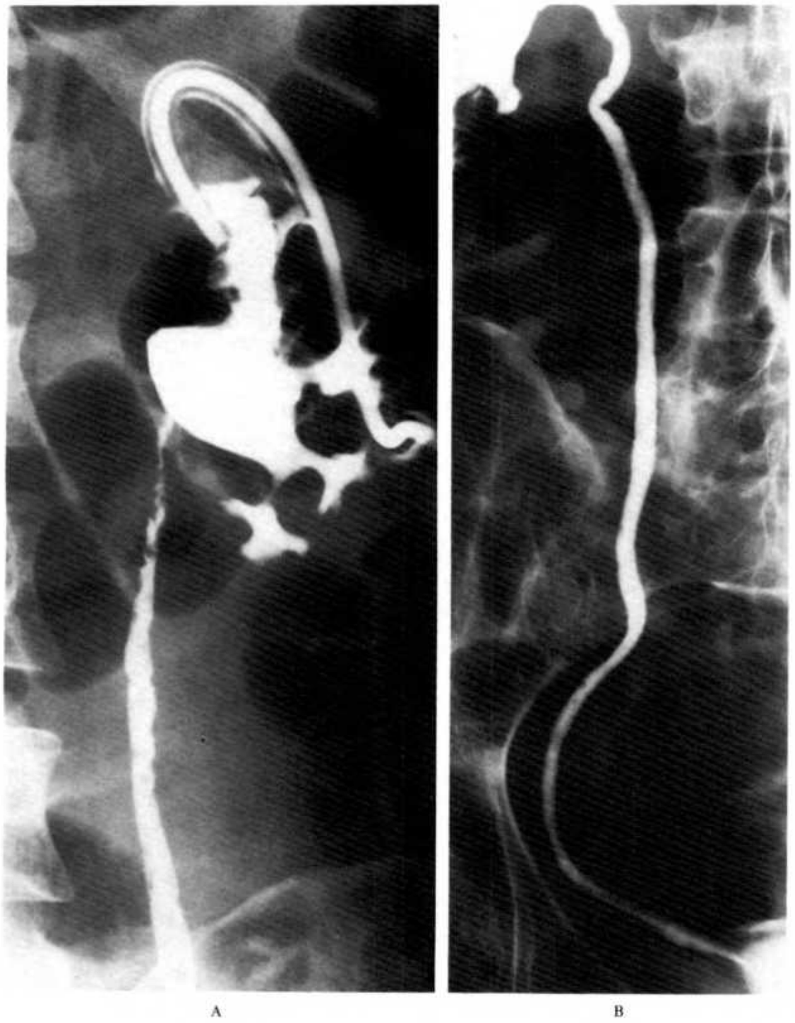

FIG. 7.

Two patients with nephrostomies and nodular filling defects in the ureter associated with infection: (A) Case 4, (B) Case 5.

are clearly remote from the tube, suggesting another mechanism. Hypersensitivity to catheter materials or chemicals used in sterilisation has been proposed as a causal factor in ureteric oedema seen with stent catheters (Levin et al, 1982). If such substances were released into the urine by nephrostomy catheters they may create changes in the ureter remote from the catheter.

In summary, multiple subepithelial filling defects in a patient with a nephrostomy tube may have one of several implications. First, they may truly represent ureteritis cystica associated with infection, so cultures are necessary. Secondly, the filling defects may represent subepithelial oedema due to direct irritation by the catheter, and should resolve with repositioning. Thirdly, they may represent a reaction to the presence of the tube itself, by a mechanism which is, at this time, unknown.

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Book review

Wilhelm Conrad Rontgen. His life and the new kind of rays By Thomas J. Deeley, pp 79, 1986 (Tenovus Cancer Information Centre, Cardiff), £1.50.

Students of radiology will find little about Rontgen's life in the average medical school library, nor do the textbooks include more than the briefest of historical introductions. Dr Deeley's purpose in writing this book is to perpetuate Rontgen's memory and to retrieve the original papers and press reports from sources which are difficult to find. This little book contains a short biography of Röntgen and his first and second papers on X rays, published in December 1895 and March 1896 and translated into English. (The text of Röntgen's third paper, published in March 1897, could have been included for completeness.) There are sections on the diagnostic and therapeutic uses of radiation and accounts of the impact of Rontgen's discovery as revealed in the scientific and popular press. Additionally, he gives us condensed chronologies of radiation science and Röntgen's life, a brief history of the *British Journal of Radiology*, the experimental background to Röntgen's discovery and the controversies about his priority, and Rontgen's influence on philately and language.

Perhaps Dr Deeley attempts too much in such a short space The intended audience is not specified, It is not likely that the subject would interest an audience without some knowledge of physics or medicine. However, the section on "The use of X-rays" is obviously an attempt to simplify the subject for a lay audience The result is confusing The explanation of the production of the X-ray image on page 24 is erroneous. It is a pity that contrast medium is called "dye" on pages 25 and 29; this word is more confusing than helpful to most patients. There are other errors of fact. Figure 11 is a positive image, while the other radiographs in the book, like those in the hospital envelope, are negatives Leyden has always been in the Netherlands (page 5) not in Germany, although the storage of an electrical charge in the so-called Leyden jar was probably discovered simultaneously in Germany by E. G. von Kleist. Every section contains errors of spelling and punctuation which could have been avoided by more careful proofreading. On the other hand, the illustrations are well chosen and well reproduced.

The volume does not attempt to be an original work, and the sources are acknowledged. Its publication is timely with the centenary of Röntgen's discovery now less than nine years away. If the book awakens a historical sense in radiology's practitioners it will have succeeded in its aim, and at this price, despite its blemishes, every radiologist and radiographer ought to purchase his or her own copy. It will cost less than the photocopies of the original documents reprinted here, and is worth its price for the reprinting of Röntgen's papers alone.

J. M. GUY

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MAY 1987

Changes in Wolfe mammographic patterns with aging

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ABSTRACT

Mammograms of 212 women were examined at a mean interval of 15 (range 11–17) years, to determine whether there was any change in Wolfe mammographic pattern with age. The mean age of the patients at repeat mammography was 52 (range 32–75) years. The DY pattern tended to change to P_2 or P_1 with age. Those in whom the DY pattern remained tended to be younger (mean age 47 years) than those who changed to P_2 (57 years), or P_1 (55 years) Women whose pattern changed from DY to N_1 had a mean age of 42 years. These findings support the hypothesis that the perilobular connective-tissue elements are the structures responsible for the dense appearance of the DY breast, as these elements would be most active between 15 and 45 years (peak reproductive period) and tend to regress later

In 1975 Wolfe (1976a) described four distinguishable mammographic patterns—N_1, P_1, P_2 and DY—which were determined by the relative proportions of fat, ductal and epithelial and connective tissues within the breast. Over 80% of his patients who developed breast cancer in a mean 30-month follow-up period had either a DY or P_2 pattern.

The same author later reported (Wolfe, 1976b) that these patterns could change with aging. In this study most breasts in the low-risk N_1 and P_1, and high-risk P_2 groups did not change over a mean 7.5-year period but 52% of DY breasts did, usually to P_2 but also in over a third of those who change, to a lower-risk pattern, either P_1 or N_1.

We report the results of radiographic follow-up over a longer period, in 212 patients who first underwent mammography between December 1967 and December 1970.

PATIENTS AND METHODS

The patients in the present study were drawn from a previously reported consecutive series of 791 women who attended a diagnostic breast clinic during the period 1967–70 (Roberts et al, 1984). Apart from 18 women who were known to have developed breast cancer, all were offered further clinical consultation and mammography, either as part of their continuing outpatient care or via a standard letter to their homes. In all, 212 patients agreed to participate and underwent mammography between November 1983 and May 1984, unless a mammogram had been performed for other reasons more recently than 1982.

The initial and repeat mammograms of all 212 women were examined and classified by a single radiologist and the results examined to determine whether there was any tendency for Wolfe patterns to change with aging.

RESULTS

The mean period from initial to repeat mammography was just under 15 (range 11–17) years and the mean age of the patients at repeat mammography was 52 (range 32–75) years.

Initially, 29 (14%) of the 212 patients were N_1, 38 (18%) were P_1, 43 (20%) P_2, and 102 (48%) DY, whereas at follow-up the proportions had changed to 33 (15.5%) P_1, 63 (29.5%) P_2, and 58 (27.5%) DY. Only 17% of N_1 and 5% of P_2 breasts changed (all to P_1) and no patient with a P_1 pattern showed a change with aging. In the DY group, however, 44 (44%) patients changed, 22 changing to P_2, 13 to P_1, and nine to N_1 (Table I).

The mean age of DY patients who remained unchanged was 47 years, whilst those who changed to P_1, P_2 and N_1 had mean ages of 55, 57, and 42 years, respectively.

DISCUSSION

Our findings correspond with those of Wolfe, showing a tendency for the DY pattern to disappear with aging and most changes being to P_2 or P_1 rather than to N_1.

TABLE I

CHANGES IN WOLFE CLASSIFICATION OVER A 15-YEAR FOLLOW-UP PERIOD

		Breast pattern in 1984			
		N_1	P_1	P_2	DY
Totals 1970					
N_1	29	24	5	0	0
P_1	38	0	38	0	0
P_2	43	0	2	41	0
DY	102	9	13	22	58
Totals 1984		33	58	63	58

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The DY women whose patterns remained unchanged were younger (mean age 47 years) than those who changed to P_2 or P_1 (mean age 57 or 55 years, respectively) and more of the patients with DY breasts may yet change over the next 10 years or more. The women with DY breasts who changed to N_1 were younger still (mean age 42 years), suggesting that breasts with a prominent duct pattern behave differently from the N_1 breast.

The tendency toward disappearance of the DY pattern with aging supports the hypothesis (Pashby et al, 1981) that the structures responsible for the dense appearance of the DY breast are the perilobular connective tissue elements, which would naturally be most active during the peak reproductive period between 15 and 45 years and tend to regress thereafter.

ACKNOWLEDGMENT

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Factors which influence the occurrence of vascular calcification in the breast

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ABSTRACT

Breast arterial calcification, as seen on mammography, increases in frequency with advancing age, especially after menopause. No association was found with systemic hypertension. The number of diabetics in the series was too small for comparative purposes. An early menopause and a history of pregnancy were factors which influenced incidence. Oral contraception was associated with a lower incidence of calcification before, but not after menopause. On the other hand, hormonal preparations taken for menopausal symptoms were associated with a lower incidence of calcification in post-menopausal women.

The incidence of arterial calcification in the breast, detected on mammography, increases with advancing age and has an association with diabetes mellitus (Baum et al, 1980; Schmitt & Threatt, 1984a; Sickles & Galvin, 1985) and possibly with systemic hypertension (Schmitt & Threatt, 1984b).

The aim of the present study is to determine whether or not hormonal factors influence the occurrence of breast arterial calcification (BAC).

METHOD

The occurrence of BAC on mammography was recorded for women over the age of 35 years who presented at a Breast Cancer Screening Unit. Women aged 31–35 years, who presented to a Breast Clinic with a variety of symptoms and subsequently underwent mammography, were included in the study in order to increase the age range of the study group. As part of the protocol for a long-term research project into risk factors and screening for breast cancer, each woman completed a detailed questionnaire concerning their menstrual, obstetric and medical history. Mammography was performed on an IGE MMX2 mammographic unit, using the Kodak Min R film–screen system.

Vascular calcifications were identified as having a linear orientation, often with parallelism, along the periphery of tapered structures whose configuration was typical of arteries and distinct from breast ducts (Fig. 1).

RESULTS

The overall incidence of BAC was 0.94% in a study population of 7435 women. The incidence gradually increased throughout the age range (Table I), especially after the age of 50 years.

TABLE I

THE INCIDENCE OF VASCULAR CALCIFICATION ON MAMMOGRAPHY, RELATED TO AGE

	Age of women (years)						
	31–35	36–40	41–45	46–50	51–55	56–60	>60
Total	1603	1452	1550	1565	1096	126	41
No. with vascular calcification	2 (0.1%)	4 (0.3%)	7 (0.5%)	17 (1.1%)	30 (2.7%)	6 (4.7%)	4 (9.8%)

$\chi^2 = 270.67$, DF 12.

A higher incidence of BAC was associated with a menopause, spontaneous or artificial, under the age of 40 years (Table II). The differences do not, however, reach statistical significance. Pregnancy was associated with an increased incidence of BAC in post-menopausal women (Table III), but there was no change in incidence with increasing number of pregnancies. There was no significant difference in BAC between those

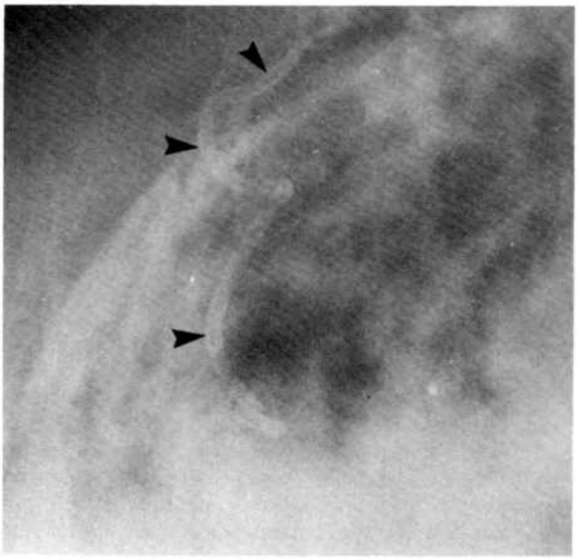

FIG. 1.

Detail from lateral portion of craniocaudal mammogram of left breast, showing arterial calcification (arrows).

TABLE II

THE RELATIONSHIP OF VASCULAR CALCIFICATION TO AGE AT MENOPAUSE

	Age at menopause (years)			
	<40	41–45	46–50	>51
Total	233	502	1242	731
No with vascular calcification	5 (2.1%)	4 (0.8%)	20 (1.6%)	9 (1.2%)

$\chi^2 = 6.29$, DF 6, $p = 0.3913$

TABLE III

THE RELATIONSHIP OF VASCULAR CALCIFICATION TO PREGNANCY IN POST-MENOPAUSAL WOMEN

	No of pregnancies		
	0	1	>1
Total	482	359	1595
No with vascular calcification	5 (1.0%)	10 (2.8%)	40 (2.5%)

$\chi^2 = 12.12$, DF 4, $p = 0.0165$.

patients who had breast fed (0.9%) and those who had not (0.4%) ($\chi^2 = 5.42$, DF 2, $p = 0.066$).

A history of oral contraception was associated with a lower incidence of BAC (Table IV), although this difference disappeared in women over 50 years of age (Table V). Breast arterial calcification was present in six (1.6%) women who gave a history of taking steroidal preparations for menopausal symptoms, either currently or in the past. This incidence of BAC was lower than that in the general population aged over 50 years.

There was no association between BAC and systemic hypertension, the incidence being 1.37% in 505 hypertensive women and 0.7% in normotensive women ($\chi^2 = 2.59$, DF 2, $p = 0.27$). Only six women were diabetic and none showed vascular calcification on mammography.

DISCUSSION

Sickles and Galvin (1985) found a significant association between BAC and advancing age. While the prevalence of BAC is substantially higher in diabetic than in non-diabetic women (Schmitt & Threatt, 1984b; Sickles & Galvin, 1985), the association with age is much more significant than that with diabetes. Hypertension may be another contributing factor to BAC, but is itself more frequent with increasing age and has an association with diabetes (Schmitt & Threatt, 1984a).

The overall incidence of BAC was 0.94% in the present series, considerably lower than the 9% of Schmitt and Threatt (1984a,b) and the 9.6% of Sickles and Galvin (1985). This difference may be attributed to the younger average age of the present series.

TABLE IV

HISTORY OF ORAL CONTRACEPTION AND THE INCIDENCE OF VASCULAR CALCIFICATION, IN WOMEN OF ALL AGES

	Oral contraception	
	No history	History
Total	4680	2535
No with vascular calcification	46 (1.0%)	6 (0.2%)

χ^2 (Yates' correction) 11.63, $p = 0.0006$

TABLE V

PAST HISTORY OF ORAL CONTRACEPTION AND THE INCIDENCE OF VASCULAR CALCIFICATION, IN WOMEN OVER THE AGE OF 50 YEARS

	Oral contraception	
	No history	History
Total	2183	304
No. with vascular calcification	36 (1.6%)	4 (1.3%)

$p = 0.81$ (Fischer exact test).

This study shows that there are hormone-related factors which influence the occurrence of BAC, including pregnancy and early menopause. Oral contraception is known to influence the parenchymal pattern in mammography (Leinster & Whitehouse, 1985) but has not previously been shown to affect calcification in the breasts. The preventive effect that oral contraception has on BAC does not persist after menopause. However, hormonal steroid preparations taken for menopausal symptoms seem to exert a protective influence in regard to BAC within the post-menopausal group. If BAC is regarded as an aging process, then hormonal preparations appear to delay this development.

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Mammographic patterns in twin pairs discordant for breast cancer

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ABSTRACT

As part of a case-control study of breast cancer in pairs of twins selected from the population-based Finnish Twin Cohort, mammograms of 30 pairs (seven monozygotic (MZ), 23 dizygotic (DZ)) discordant for breast cancer were analysed. The mammographic pattern in the unaffected breast of the cancer case was compared with the pattern in the ipsilateral breast of the healthy twin (control). There were no differences for MZ pairs, while among DZ pairs the cancer case had a prominent parenchymal pattern significantly more often than the control, as assessed by two radiologists independently and blindly. Thus, there is a relationship between parenchymal pattern and risk of breast cancer even when the controls are the twin sisters of breast-cancer cases and are themselves at high risk The overall similarity, despite disease discordance, in parenchymal pattern of the twins (more evident among MZ than DZ pairs) suggests a familial, possibly genetic influence on parenchymal pattern

The parenchymal pattern in mammograms as classified by Wolfe (1976) has been claimed to be associated with risk of breast cancer (Wolfe, 1976; Wolfe et al, 1982; Gravelle et al, 1986) as well as with other risk factors for breast cancer (Brisson et al, 1984). A recent, multivariate analysis indicated that parenchymal pattern is a risk factor for incident breast cancer, even after adjusting for other known risk factors (Whitehead et al, 1985). The concept of association between risk of breast cancer and parenchymal pattern has been challenged by other studies (Moskowitz et al, 1980; Tabar & Dean, 1982) and the reproducibility of mammographic classification has been criticised (Myers et al, 1983).

Family history is a consistent risk factor for breast cancer, indicating that genetic factors may also play a role (Kalache & Vessey, 1982). Family studies have suggested that a small proportion of breast-cancer cases are of genetic aetiology (Williams & Anderson, 1984). The population-based Danish twin study (Holm et al, 1982) indicated no difference in the concordance rate for breast cancer between MZ and DZ pairs As part of a case-control study of breast cancer in twins, we have investigated the relationship of mammographic parenchymal pattern to risk of breast cancer.

SUBJECTS AND METHODS

Female twin pairs with breast cancer were identified by linkage of the Finnish Twin Cohort data with the Finnish Cancer Registry (Kaprio et al, 1981). Linkage covered incident cases between 1967 and 1982 All pairs with either twin alive in 1983 were invited to participate in the study Twins aged more than 70 years were excluded The study protocol consisted of an interview focusing on dietary factors (to be reported elsewhere), clinical examination (by A.A.), mammography and drawing of a venous blood sample. For 32 pairs both members completed the protocol. One pair in which bilateral breast cancer occurred in one twin and one breast-cancer-concordant pair were excluded from these analyses; the final number of pairs was thus 30: seven monozygotic (MZ) and 23 dizygotic (DZ).

Lateral oblique mammograms of good quality were taken using a dedicated mammographic unit (Mamex, Palomex OY) both members of a twin pair were imaged on the same unit, generally on the same day. For cancer cases the unaffected breast was imaged, while both breasts of the unaffected twin were imaged. For each pair the mammogram of the unaffected breast of the cancer twin and the corresponding mammogram of the twin (ipsilateral breast) were analysed. Two radiologists, blind to disease status and twin-pair zygosity or other study variables, examined the mammograms. The parenchymal pattern was classified according to Wolfe (1976) as N, P1, P2 or DY. The difference in distributions between cancer patients and their twins (regarded as controls) was tested using McNemar's test for matched-pair data (Dixon et al, 1981). The reliability of the mammographic classifications was computed using the reliability coefficient (kappa) (Dixon et al, 1981).

RESULTS

Reliability analysis

The kappa coefficient was 0.64 when all mammograms were considered. The kappa coefficient for the cancer cases was 0.70 when all four categories of Wolfe's classification were used and 1.0 when N and P1 categories were pooled. The corresponding coefficients were 0.56 and 1.0 for the controls Thus, the difference between radiologists was due to differences in classifying P1 and N cases.

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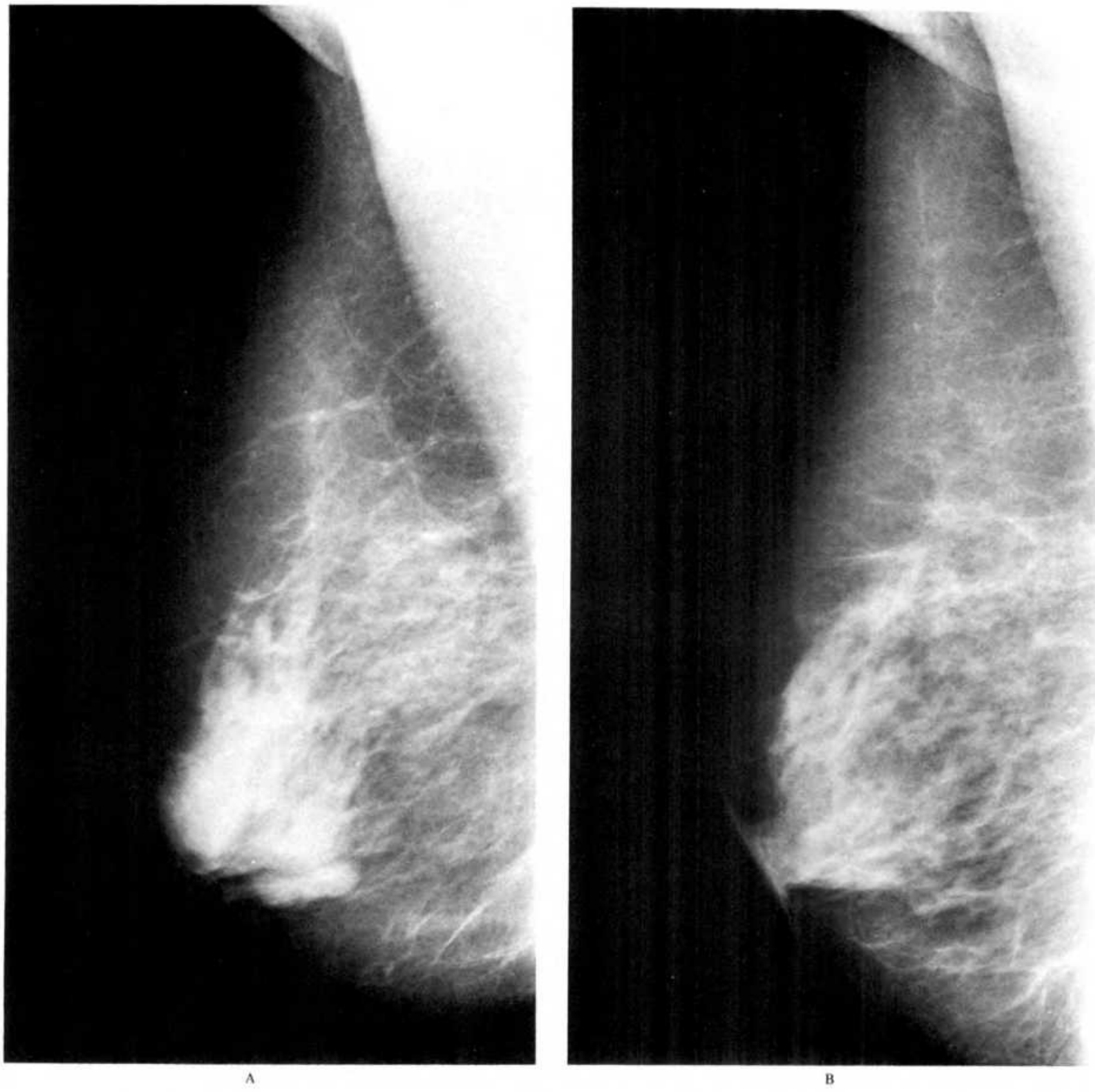

FIG. 1.

Mammograms of a monozygotic twin pair discordant for breast cancer. (A) Unaffected right breast of cancer twin and (B) right breast of the healthy twin.

Parenchymal pattern

The parenchymal pattern distribution in the cases and controls of the MZ and DZ pairs is shown in Table I.

Radiologist 1. Among the MZ twins, the cancer-case breast had more severe changes than the control breast in one pair, while the parenchymal pattern was the same in the remaining six pairs (Fig. 1). Among DZ twins, eight pairs had similar parenchymal patterns. The cancer-case breast had more severe changes than the control breast in nine pairs, while the converse was true in six pairs (a relative risk for the parenchymal pattern in relation to breast cancer of 1.5, $p = 0.39$). Combining the results for MZ and DZ pairs resulted in a relative risk of 1.67 ($p = 0.26$).

Radiologist 2. Among the MZ twins, the cancer-case breast had more severe changes than the control breast in one pair, while for the remaining six pairs the parenchymal pattern was the same. Among DZ twins, 15 pairs had similar parenchymal patterns. The cancer-

TABLE I

Classification of parenchymal pattern in the unaffected breast in cancer cases and the ipsilateral breast of healthy twins (control)

Control	Cancer case							
	MZ				DZ			
	N	P1	P2	DY	N	P1	P2	DY
Radiologist 1								
N	2	0	1	0	2	6	1	0
P1	0	3	0	0	6	4	2	0
P2	0	0	1	0	0	0	1	0
DY	0	0	0	0	0	0	0	1
Radiologist 2								
N	3	0	1	0	7	5	2	0
P1	0	2	0	0	0	6	1	0
P2	0	0	1	0	0	0	1	0
DY	0	0	0	0	0	0	0	1

case breast had more severe changes than the control breast in eight pairs, while the opposite was true for none (relative risk >8, $p = 0.046$). Combining the data for MZ and DZ pairs gave a ratio of nine cases with more severe changes in the cancer twin against no cases with the reverse being true ($p = 0.029$).

It should be noted that if the classification is dichotomised as N+P1 versus P2+DY, both radiologists classified all pairs in the same way For this dichotomous classification, the tetrachoric correlation between twins for MZ and DZ pairs combined was 0.79 (standard error = 0.14).

Discussion

There appeared to be no difference in parenchymal pattern between MZ twins with and without breast cancer. The very small number of MZ pairs must of course be taken into account. For DZ pairs, on the other hand, the non-diseased breast of the twin with cancer had a prominent parenchymal pattern significantly more often than the corresponding breast of the unaffected twin. The overall correspondence in the classification of the mammograms by the radiologists was satisfactory, and discrepancy was due to differences in the classification of N and P1 patterns. Because the classification of the mammograms was based on the unaffected breast of the cancer cases, the proportion of P2 and DY cases is smaller than that in studies classifying parenchymal patterns in breasts in which cancer occurs.

This study suggests that the relationship of parenchymal pattern to breast cancer is present even when controls are the sisters of breast-cancer cases, themselves at high risk of breast cancer. The similarity in parenchymal pattern of the twins, more evident among MZ than DZ pairs, suggests a familial, possibly genetic influence on parenchymal pattern. Parenchymal patterns have been found to be more similar in mother–daughter and sister pairs than in control pairs of non-related individuals in a hospital-based series (Wolfe et al, 1980). The genetics of parenchymal pattern could be studied as part of a mammographic screening study in a normal population.

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Book review

A Radiographer's Handbook of Hospital Practice. By D. N. Chesney and M. O Chesney, pp vii+129+index, 1986 (Blackwell, Oxford), £5.95
ISBN 0-632-01487-3

This reviewer confesses to a mistrust of books which hint at being condensed, handy pocket-reference versions of fuller length texts The risk in reading or recommending them concerns passive acceptance of facts and conclusions, without a care for underlying explanations and arguments. This book is free of such faults. The authors acknowledge the influence of their fuller *Care of the Patient in Diagnostic Radiography* but their new work emerges with an identity of its own.

In content, the book covers the related section of the College of Radiographers' DCR Syllabus. The style is easy but authoritative and written from depth of both radiographic experience and knowledge of the literature There are no illustrations, a point which may restrict the book's appeal to a beginner, but encouragement is given throughout for the reader to consider the various topics in their clinical settings, where the opportunity to see and handle is so much more valuable than figures on a page.

The book is addressed mainly to diagnostic radiographers and students, although the basic nursing techniques are equally relevant to radiotherapy, about one-third of the book concerns imaging procedures. These range from the nearly extinct bronchography (concern to follow the DCR syllabus is responsible for this inclusion) to computed tomography, ultrasound and radionuclide imaging. One unfortunate consequence of the syllabus link is a chapter devoted to the Ten-Day Rule but, even so, comprehension of the principles it describes is transferable to more recent legislation.

To summarise, the book can be strongly recommended for purchase by diagnostic radiography students because of its sound theoretical support to practical learning. It will, no doubt, appear in libraries in schools of radiography, but its value to the learner will be realised better if it is accessible from the pocket rather than the shelf

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Variation in repeat rates between 18 radiology departments

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ABSTRACT

A comprehensive analysis of repeat rates has been obtained from an observational study of radiological practice in diagnostic X-ray departments throughout Wales. Interdepartmental and intradepartmental repeat rates are investigated for chest, abdomen, pelvis, sinus, lumbar spine, cervical spine and intravenous pyelographic examinations. The confounding effects upon observed repeat rates of trainee practitioners and automatic exposure control devices are also considered. The overall proportions of total film cost and patient exposure attributable to repeat radiographs are estimated to be 10% and 14% respectively.

Production of diagnostic radiographs involves well defined procedures. However, one or more of the radiographs produced during an examination may be of insufficient quality to demonstrate the required anatomical features. Patients may then be re-irradiated to obtain the desired image quality and thus receive higher doses than would normally be required for that particular examination. It has been estimated that one patient in six undergoing a diagnostic examination has at least one film retaken (Berry & Oliver, 1976). It is important to evaluate the frequency of such repeat radiographs and to ascertain the principal reasons for their cause, in order that excess exposure of patients and consequent carcinogenic risk be minimised. The financial burden to the NHS of repeat films must also be considered. If one in 10 radiographs was repeated then the annual cost of repeat films would be £3–£4m (Wrighton & Oliver, 1980).

Repeat rates are calculated as the ratio of the number of repeated radiographs to the total number of radiographs taken. However, the denominator in this calculation has differed in previous studies, rendering direct comparisons difficult. Chu et al (1982) defined the denominator as the product of the number of examinations performed and the average number of films used during the examination, whereas Mazzaferro et al (1974) simply used the total number of radiographs of acceptable quality.

Methods of determining repeat rates, and indeed of deciding which radiographs should be repeated, have also differed in previous studies. One method utilised a single quality controller at the film processor output whose purpose was to identify and record those radiographs which required repetition (*e.g.* Goldman et al, 1977). Alternatively, the practitioners undertaking the examinations decide which radiographs to repeat.

Previous studies have been undertaken for time periods of between 4 weeks and 2 years. A recent investigation demonstrated that repeat rates may depend upon the period of observation as there can be large weekly variations (Watkinson et al, 1984). However, a previous study showed no such variation; the weekly repeat rates of a 12-week period did not differ significantly from the means of two 6-week periods (Goldman et al, 1977).

Typically, reported repeat rates have ranged from 3.8% (Chu et al, 1982) to 11.6% (Watkinson et al, 1984). Although some of this variation may be due to differences in the manner in which repeat rates are estimated, other factors are also important. Berry and Oliver (1976) demonstrated a threefold variation in repeat rates between hospitals of different types (*i.e.* a district general hospital and a private nursing home). The relative contributions to the repeat rate of a department from trainee radiographers and automatic exposure control (AEC) devices have not previously been fully investigated. It has been assumed that the presence of student radiographers increases the overall repeat rate (McKinlay & McCauley, 1977) and it has been demonstrated to a limited extent that the use of AEC devices reduces repeat rates (Faulkner et al, 1986).

Using data collected from this study, it has been possible to investigate repeat rates within 18 major radiology departments. The initial aim of the repeat analysis was to identify those frequently performed examinations with high repeat rates and to ascertain the major causes of such re-exposure of patients. The financial cost and excess patient exposure derived from repeated radiographs was also estimated.

METHOD

A comprehensive study of radiological practice within diagnostic radiology departments throughout Wales is being carried out under the auspices of the Royal College of Radiologists and the College of Radiographers. The examinations investigated are listed in Table I. These were chosen because they are frequently performed examinations (Kendall et al, 1980). Repeat rate was simply defined as the ratio of the number of repeated exposures to the total number of

TABLE I

PERCENTAGE OF REPEATED FILMS ATTRIBUTABLE TO EACH REASON FOR SEVEN TYPES OF EXAMINATION

Reason	Examination							
	Chest	Abdomen	Pelvis	Sinus	L-Spine	C-Spine	IVP	Overall
Underexposure	56	26	21	21	30	23	33	33.1
Overexposure	20	21	38	0	11	0	15	14.4
Movement	0	26	0	0	7	9	3	6.0
Position	18	16	33	57	46	50	24	36.3
Developing	0	0	4	0	0	0	0	<1.0
Equipment	0	0	0	7	1	0	6	1.4
Other	6	2	4	14	5	18	18	8.5
Overall	10.7	9.5	10.8	8.8	15.1	7.5	5.2	10.2

exposures. Radiographs which served to provide additional information, that is, through non-standard projections, were not deemed repeats, although those which provided improved information due to the poor quality of an original radiograph (even if both radiographs were sent for reporting) were identified as repeat radiographs. In all cases the decision to repeat a radiograph was made by the practitioner conducting the examination, although a senior member of staff was consulted in doubtful cases. This is believed to be common practice within radiology departments throughout the UK.

Previous observational studies have suffered from observer bias; practitioners often reported on their own repeated radiographs. The present study overcomes this bias since all of the data were recorded by an independent observer. Further, the staff of each department, although informed as to the aims of the overall study of radiological practice, were not made fully aware of the investigation of repeat rates. Thus, any effect of the observer's presence upon repeat rates was thought to be minimal.

The average observation period within each radiology department was 5 weeks. For each radiograph, information was recorded on the examination and projection type, the film size and type, the exposure of the patient and, where necessary, the reason for repeating the radiograph. The status of the practitioner (student or qualified staff) and use of automatic exposure control devices were also recorded. Details of the film type and size were used to estimate the financial cost of the examinations observed, and excess exposures attributable to repeat radiographs were estimated from the data.

The causes of repetition identified are given in Table I. "Movement" refers to that of the patient which occurred during the exposure, "development" refers to that directly attributable to an error in film processing and "equipment" refers to any other equipment failures. The group "other" contained such reasons as severely fogged film and items of radio-opaque clothing left on the patient, obscuring the areas of interest. This group will be discussed more fully in the following section.

The results were derived from 50 X-ray rooms in 18 radiology departments and are presented within the following section in two parts. The first considers the causes of repeating particular examinations and the interdepartmental and intradepartmental variations in observed repeat rates. The latter part examines repeat rates associated with trainee practitioners and AEC devices and estimates the contribution of these two factors to overall departmental repeat rates.

RESULTS

The total number of radiographs observed for the examinations listed in Table I is 2781, and the total number of repeated exposures in 284. The overall repeat rate is thus 10.2%. The maximum overall repeat rate for any examination is 15.1%, associated with lumbar-spine examinations, and the minimum is 5.2%, associated with intravenous pyelography (IVP). The primary reason given for repeating radiographs was patient positioning, although underexposure was also a frequently described cause. Repeating a radiograph due to an error in film processing occurred infrequently, only one such case was recorded throughout the study.

Each examination type consists of at least one projection. Of interest is the variation in repeat rate for each of these projections as shown in Table II. It has been found that there is no significant difference between the postero-anterior (PA) and lateral projections of chest examinations ($\chi^2 = 0.17$, $p > 0.5$). Also, the three standard cervical-spine projections (lateral, antero-posterior (AP) and supine view to show the odontoid process (OP)) have associated repeat rates which do not differ significantly ($\chi^2 = 0.37$, $p > 0.5$). However, supine views (AP) of the abdomen are repeated with almost twice the frequency of erect views and the occipito-mental projection (OM) of sinus examinations have a repeat rate twice that of the occipito-frontal (OF) and lateral projections. Forty-three per cent of all repeated radiographs from lumbar-spine examinations are associated with the lateral

TABLE II

REPEAT RATES FOR EACH EXAMINATION PROJECTION

Examination	Projection	Mean repeat rate × 100
Chest	PA	10.7
	Lateral	12.5
Abdomen	AP	9.9
	Erect	5.9
Pelvis	AP	10.7
Sinus	OM	13.1
	OF	6.1
	Lateral	6.1
Lumbar spine	AP	10.7
	Lateral	19.6
	Lumbosacral joint	14.9
Cervical spine	Lateral	8.8
	AP	6.7
	OP	7.5
IVP	Control	11.5
	Immediate	6.2
	3–5 min	4.2
	10 min	4.2
	15 min	1.6
	20 min	3.8
	FFL	4.2
	FL BLDR	2.7
	Post-micturition	3.3

FFL = final full length radiographs, FL BLDR = radiographs of the full bladder

TABLE III

DEPARTMENTAL REPEAT RATES

Department	% repeat rate	Range of % repeat rates
1	13.8	5.3–18.1
2	11.9	7.1–17.7
3	10.8	9.1–11.5
4	3.5	3.2– 4.2
5	10.9	4.4–25.0
6	8.9	1.2–13.9
7	11.9	<4.4–15.8
8	14.0	<3.1–32.4
9	14.1	8.7–19.2
10	9.3	6.6–28.0
11	4.8	1.7– 7.6
12	10.9	7.1–12.0
13	12.2	2.3–16.5
14	13.6	12.1–14.6
15	10.4	5.0–18.2
16	19.3	17.4–20.5
17	5.6	<3.8– 7.3
18	4.2	1.4– 6.7

projection whereas only 24% are associated with the AP projection. Of IVP examinations, 11.5% of initial (control) radiographs are repeated, whereas only 1.6% of those radiographs produced 15 min after injection require repetition.

Table III lists repeat rates for each of the radiology departments studied. These are averaged over all of the X-ray rooms within any department during the observation period. The final column of Table III indicates the maximum and minimum values of repeat rate observed for all rooms of a department. No estimate of weekly variations in repeat rates is made. All the departments consisted of two or more X-ray rooms. The minimum departmental repeat rate is 3.5% and the maximum is 19.3%. The largest intradepartmental variation is < 3.1% to 32.4% and the smallest is 3.2% to 4.2%. An attempt to explain these variations will be made in the next section.

The information thus far presented is repeat rates which are, on the whole, confounded by the presence of trainee practitioners and/or by the use of AEC devices. Of all the repeated films observed, 14.4% derive from student radiographers and 2.8% are attributable to procedures utilising AEC devices. Table IV is a summary of repeat rates for qualified staff, student radiographers and procedures involving AEC devices.

The departments can be classified into four types according to how the radiographs were produced.

1. Those departments in which the radiographs were produced by qualified staff only (four departments).
2. Those departments in which the radiographs were produced by qualified staff and student radiographers (eight departments).
3. Those departments in which the radiographs were produced by qualified staff and AEC devices (three departments).
4. Those departments in which the radiographs were produced by qualified staff, student radiographers and AEC devices (three departments).

In all but one examination the AEC devices were operated by qualified staff. The effects of trainee practitioners and AEC devices upon overall repeat rates are demonstrated in departments of Type 2 and Type 3 by comparison of Tables III and IV.

The repeat rates given in Table IV are calculated from the ratio of the number of radiographs repeated by each group to the total number of radiographs produced by each group. For example, in the first department 20.4% of all radiographs produced by student radiographers are repeated radiographs.

Of the radiographs repeated by student radiographers, 44% are due to positional errors and 39% are due to underexposure. Thirty per cent of all radiographs from sinus examinations undertaken by student radiographers are repeated, as are 23% of radiographs from lumbar-spine examinations. Also, of the examinations undertaken by student radiographers, the distribution of repeat rates between projections is similar to that described previously (see Table II). The overall repeat rate associated with AEC devices is relatively low

TABLE IV

PERCENTAGE REPEAT RATES FOR QUALIFIED STAFF, STUDENT RADIOGRAPHERS AND AEC DEVICES WITHIN EACH DEPARTMENT

Department	Qualified staff	Trainees	AEC
1	12.8	20.4	NO
2	15.8	NO	10.4
3	10.1	40.0	NO
4	3.5	NO	NO
5	10.9	NO	NO
6	4.9	31.4	10.0
7	12.9	50.0	<4.8
8	14.3	<33.3	NO
9	12.3	19.4	NO
10	9.0	14.3	NO
11	5.0	<11.1	NO
12	10.2	15.0	NO
13	16.5	NO	2.3
14	13.6	NO	NO
15	11.1	7.4	NO
16	19.3	NO	NO
17	3.5	20.0	<12.5
18	4.3	NO	3.7
Overall	9.7	19.5	5.1

NO = no cases recorded during the observation period.

(5.1%) although, surprisingly, 50% of these repeated radiographs are due to incorrect exposure. Of the examinations utilising AEC devices, 38% were of chest, 21% were of pelvis and 14% were of abdomen, lumbar spine and IVP; AEC devices were not used during any of the sinus or cervical-spine examinations observed.

A detailed investigation was made of the classification "other", given as a reason for repeating a radiograph. This reveals that 34% of such cases are caused by various items of clothing left on the patient for the duration of the exposure, or the film cassette being in an incorrect position when the exposure was made. Fifty-eight per cent of this class can be regarded as being a direct result of incorrect radiographic practice. Of interest are those occasions when an exposure is made in the absence of radiographic film. The overall frequency of such an event is 1.5%, which is comparable to the repeat rate due to an equipment failure. Previous repeat-rate studies would have ignored such events. However, such cases are important only in terms of increasing patient exposure: no additional film costs are incurred.

DISCUSSION

It is shown in Table I that there is no significant difference in repeat rates between examinations of the chest, abdomen and pelvis ($\chi^2 = 0.28$, $p > 0.5$). Each of these examinations essentially involves a single film; the procedures are relatively simple and performed relatively frequently Radiographs resulting from IVP examinations are repeated with the lowest frequency (5.2%). We concur with Watkinson et al (1984) that the reason for this lies in the nature of the examination. A simple radiograph, of adequate image quality, is initially obtained which allows the position of the patient to be verified and the correct exposure factors (kV, mAs) to be established. This reasoning is supported by a closer investigation of repeat rates associated with each IVP projection. Fifty-four per cent of repeated IVP radiographs are from the initial "control" radiograph or those obtained immediately after injection of contrast medium. Repeat-rate values generally decrease as the examination proceeds. Of interest is the fact that all cases of repetition due to the absence of a radiographic film are associated with IVP examinations.

Radiographs associated with lumbar-spine examinations are repeated at a rate of 15.1% The primary reason given is that of poor patient position and 43% of the repeated radiographs derive from the lateral projection. An improved positioning technique for this particular projection would certainly alleviate this problem in all radiology departments; 20% of all repeated radiographs were attributable to this examination projection.

Repeat rates given in the final column of Table III indicate large intradepartmental variations in repeat rates. Such variations have previously been observed by Watkinson et al (1984) although the magnitude of the variations in the Watkinson study is very much less than that observed in several of the departments investigated in the present study. In previous studies, intradepartmental repeat rates have been explained in terms of X-ray room utilisation (rooms dedicated to IVP examinations will show lower repeat rates than general-purpose rooms), the frequency with which a room is used (*i.e.* the familiarity of staff with equipment), and persistent or recurrent machine faults in a particular room. The present study involved only the most frequently used X-ray rooms within a department and the low frequency of repeated radiographs due to machine failure indicates that no X-ray set was prone to such problems during the study period. The intradepartmental variations demonstrated by this study can be entirely explained by three factors. the frequency distribution of examinations within a room, the presence of trainee radiographers undertaking examinations within a room, and the use of AEC devices. To illustrate, consider Department 7 (Table III), which comprised three X-ray rooms with repeat rates of < 4.4%, 9.1% and 15.8%. The room with the lowest repeat rate was dedicated to IVP examinations and utilised an AEC device. The room with an associated repeat rate of 15.8% was used for general radiology but was observed during a period when student radiographers undertook examinations. Finally, a repeat rate of 9.1% was derived from a general X-ray room; no AEC devices were utilised and only qualified staff undertook examinations.

Interdepartmental variations in repeat rates are more difficult to explain; they have also been demonstrated by previous studies (*e.g.* Berry & Oliver, 1976) and explained in terms of the types of department and workloads. Table III illustrates the overall repeat rates of each department, three of which have repeat rates less than 5% and three have repeat rates of greater than 14%. The remaining departments show similar repeat rates regardless of the type of department.

Table IV illustrates the effect of trainee practitioners and AEC devices on repeat rates. The overall repeat rate associated with student radiographers (19.5%) is twice that of qualified staff, whereas repeat rates associated with AEC devices is half (5.1%). Although this trend was expected, qualitative demonstration has previously been inadequate.

Comparison of Tables III and IV demonstrates that, in departments of Type 2 (see previous section), there are no significant differences ($\chi^2 = 0.00$–0.17, $p > 0.5$) between the overall departmental repeat rate (Table III) and that derived from the qualified staff only (Table IV). This shows that the presence of student radiographers does not affect the overall repeat rate of these departments. This is due to the relatively small number of examinations undertaken by student radiographers within these departments. For example, in Department 12, only 20 of the total 138 radiographs recorded were produced by student radiographers.

The effect of AEC utilisation upon overall departmental repeat rates can be demonstrated by considering departments of Type 3; the overall repeat rates associated with Type 4 departments may be confounded by the presence of student practitioners. The overall repeat rates of Type 3 departments do not differ significantly from the repeat rates associated with the qualified staff within these departments ($\chi^2 = 0.00$–0.91, $p > 0.3$). Thus, the use of AEC devices has no apparent effect upon the overall repeat rates of these departments. This is due to the relatively infrequent use of AEC devices. For example, within Department 13, of the total 147 radiographs produced, 44 were obtained using an AEC device and only one of these radiographs was repeated. Therefore the repeat rate associated with the AEC device is derived from a number of observations which is insufficient to effect any significant change in the overall repeat rate of the qualified staff within the department.

An attempt to determine the financial costs and additional patient exposures derived from repeated radiographs is illustrated in Table V. The financial costing is estimated in terms of film costs alone. Of the total cost of X-ray film for the examinations observed, 10% derives entirely from repeated radiographs. It would be most cost-effective to reduce the frequency with which a radiograph is repeated in examinations of the lumbar spine. A halving of the repeat rate of this examination alone would result in a saving of approximately £20 per hundred examinations or, nationally, £124 000 per annum. Of the total patient exposure for all of the examinations observed, 14% derives from repeated radiographs. As with film costs, a reduction in the repeat rate associated with lumbar-spine examinations would be most effective in reducing this excess patient exposure: almost 20% of repeat exposure is attributable to repeated lumbar-spine radiographs.

TABLE V

THE PROPORTION OF TOTAL FILM COSTS AND PATIENT EXPOSURES ATTRIBUTABLE TO REPEAT RADIOGRAPHS

Examination	% of film costs arising from repeated films	% of patient exposure due to repeated films
Chest	10.8	8.9
Abdomen	9.5	12.9
Pelvis	10.9	12.7
Sinus	10.1	11.7
Lumbar spine	14.7	17.4
Cervical spine	7.3	5.7
IVP	5.5	8.2
All	10.2	13.9

CONCLUSION

The results presented form a comprehensive study of repeat rates thought typical of general UK practice. It has been demonstrated that the presence of student radiographers and use of AEC devices markedly affects intradepartmental repeat rates. This is as a result of AEC devices having an overall repeat rate half that of qualified staff and trainee radiographers repeating films generally with twice the frequency of qualified staff.

However, contrary to popular beliefs, the use of AEC devices or the presence of student radiographers may have no apparent effect upon the overall departmental repeat rates when random data samples are collected from radiology departments. For the departments considered in the present study, it is estimated that a threefold increase in the frequency of AEC utilisation would be necessary to effect a significant reduction in overall departmental repeat rates and a corresponding tenfold increase in student workloads would be required to produce a significant increase in overall departmental repeat rates.

It has been suggested that there is a baseline level of repeat rate, below which radiographic quality is sacrificed and further reduction in repeat rates is not cost-effective. Considering the repeat rates in Table II, it is believed that this baseline repeat rate is approximately 5% (although three departments reported repeat rates below this). Reducing repeat rates to such a level would require two-thirds of the departments studied to effect some change. The regular use of calipers to determine patient size and exposure charts to maintain consistent output would contribute to any reduction, as would the increased use of AEC devices. The cost-effectiveness of AEC devices has been discussed previously: McKinlay and McCauley (1977) estimated that the saving in film costs alone would be sufficient to cover the costs of these devices. If repeat rates were reduced to 5% in all the departments investigated, then an overall saving of 50% would be made in repeat film costs and total patient exposures would decrease by 10%.

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The cribriform plate: a sanctuary site for meningeal leukaemia

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ABSTRACT

Cranial irradiation is an effective prophylactic treatment for subclinical meningeal infiltration in lymphoblastic leukaemia. However, central nervous system (CNS) relapse still occurs in 6–10% of cases overall and in as many as 30% of cases with a poor prognosis in some series. These recurrences may be due in part to inadvertent underdosage of the cribriform plate, which is centrally situated between the orbits and is projected over their upper third in a lateral view. The dose to the adjacent meninges may thus be reduced by shielding of the radiosensitive lenses. This problem is exacerbated if conventional lateral fields centred on the mid-skull are used, because the eyes will not then project over one another. If the field centre is moved to the edge of the orbit, this problem of beam divergence can be overcome. Central axis beam blocking of both lenses is then possible, and in some patients the cribriform plate can be adequately irradiated. However, in most children the geometry of the orbit is such that it is necessary to add an anterior electron beam to ensure homogeneous dosage. These refinements in irradiation technique might prevent meningeal relapse with a lower whole-brain dose and, hence, fewer neuropsychological sequelae. This hypothesis could be tested in a clinical trial.

Once effective systemic chemotherapy had been developed for acute lymphoblastic leukaemia of childhood, it became clear that meningeal relapse occurred in 80% of patients and posed a major obstacle to cure (Bleyer, 1983, George et al, 1985). Craniospinal irradiation was then introduced and was shown in two clinical trials to be an effective prophylactic treatment for subclinical meningeal infiltration (Simone et al, 1972; Medical Research Council (MRC) Working Party, 1973). Cranial irradiation combined with intrathecal methotrexate (ITMTX) is also effective and is the standard regimen used in the United Kingdom (Chessels, 1985). The overall incidence of central nervous system (CNS) relapse is now 6–10% (Nesbit et al, 1981a, b; Komp et al, 1982, Sullivan et al, 1982, Freeman et al, 1983, George et al, 1985), but it still occurs in 20–30% of high-risk cases, with a presenting white-cell count in excess of 50 000 (Nesbit et al, 1981a, b; George et al, 1985).

Several adverse effects of cranial irradiation have been identified. Six to 12 weeks after treatment a transitory syndrome of somnolence occurs (Freeman et al, 1973). Growth-hormone deficiency (Shalet et al, 1976), abnormalities on computed tomography (CT) (Peylan-Ramu et al, 1978), and learning difficulties (Eiser, 1978; Meadows et al, 1981) have been reported in some studies, but not in others (Soni et al, 1975; Day et al, 1978). More recent work has shown that learning difficulties are more marked when cranial irradiation is part of the prophylactic regimen (Rowland et al, 1984), particularly if children under the age of 3 years are treated (Jannoun, 1983).

Attempts have been made to reduce the toxicity of prophylactic treatment by eliminating cranial irradiation. It has been clearly established that ITMTX alone is inadequate as there is an overall CNS relapse rate in excess of 40% (Green et al, 1980). Intermediate-dose MTX given systemically and combined with ITMTX was more successful but CNS relapse was observed in 20% of cases in one series (Freeman et al, 1983) and in high-risk cases a CNS relapse rate of 50% has been reported (Green et al, 1980). However, this regimen may be less neurotoxic in the long term (Eiser, 1978), and such chemotherapy can favourably influence the haematological relapse rate and, hence, overall survival (Green et al, 1980; Freeman et al, 1983). Triple intrathecal therapy is also effective in preventing CNS relapse but involves a long course of treatment and its late effects have not yet been reported (Komp et al, 1982; Sullivan et al, 1982). If prophylactic treatment of the CNS is unsuccessful then the outlook is poor. Eighty per cent of children who have an isolated CNS relapse die or suffer a further relapse (George et al, 1985), and the morbidity of retreatment of the CNS is considerable (Ochs et al, 1985).

Irradiation is used to treat the brain and its meninges because systemic chemotherapy cannot usually eradicate leukaemic cells protected by the blood–brain barrier (Bleyer, 1983). If irradiation is to be effective, an adequate dose must be delivered to the whole of the volume at risk. Because cure of the patient depends on killing every last leukaemic cell, any area of underdose will be critically important because it may permit relapse.

HYPOTHESIS

It is proposed that underdosage in the region of the cribriform plate may account for a proportion of CNS relapses in lymphoblastic leukaemia. Because these patients present with generalised meningeal leukaemia it is not usually possible to establish the initial site of relapse. By contrast, medulloblastoma is a radiosensitive brain tumour whose recurrences grow as solid

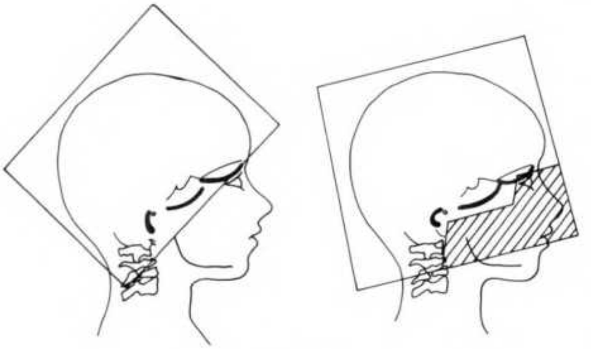

Fig. 1.

Lateral fields used for cranial irradiation. Both extend well beyond the cranium and cover the dural extensions over the facial nerve, temporal lobe and retro-orbit. In both cases the dose to part of the cribriform plate may be reduced by the shielding used to protect the lens.

masses. It seeds throughout the cerebrospinal fluid but can be cured by craniospinal irradiation. The most common site of relapse is at the primary site in the posterior fossa (Jereb et al, 1982). Subfrontal recurrence is relatively rare, occurring in 15% of cases in one series (Jereb et al, 1982), but seven cases have now been documented in the region of the cribriform plate and related to a reduced radiation dose caused by inappropriate shielding (Hardy et al, 1978; Jereb et al, 1981).

CONVENTIONAL CRANIAL IRRADIATION

The techniques of cranial irradiation evolved from those used palliatively, in which the prime aim was to provide a simple treatment which would relieve symptoms without causing side effects (D'Angio et al, 1959). The initial studies of prophylactic radiotherapy used fields which barely covered the meninges at the base of the brain: early CNS relapse occurred in one out of 15 and 12 out of 24 patients (Kim et al, 1972; Simone et al, 1972). These variable results were attributed to the low dose of irradiation (12 Gy), and in subsequent studies this was increased to 24 Gy. In addition, the radiation fields were enlarged to ensure inclusion of the meninges at the base of the brain and over the temporal lobe (Hustu et al, 1973). Meningeal relapse then occurred in only 8% of patients treated prophylactically, compared with 65% not so treated in a randomised trial (Simone et al, 1972). This result was confirmed in an MRC study in which relapse occurred in 1% of patients given craniospinal irradiation and in 32% of control patients (maximum follow-up of 2 years) (MRC Working Party, 1973). Low relapse rates of 10% were also obtained using cranial irradiation and ITMTX (Simone et al, 1972); this regimen has become part of standard therapy in the United Kingdom (Chessels, 1985).

Cranial irradiation is now conventionally given using two parallel opposed beams of X rays which treat the brain from either side. In order to include the meninges and all their extensions, the field encompasses the skull anteriorly, superiorly and posteriorly, and should have a margin of at least 2 cm to avoid underdose at the beam edge (Chang et al, 1969; Dritschilo et al, 1976). Inferiorly the field extends down to the second cervical vertebra and is shaped to spare the face, particularly the lens of the eye, because low doses of X rays can induce cataract (Merriam & Focht, 1958). The field should include the temporal lobe and floor of the middle fossa (Green & George, 1970), the posterior half of the optic globe to cover the dural extension along the optic nerve (Hustu et al, 1973), and the facial nerve up to its exit from the styloid foramen (Fernandez & Sutow, 1973). Figure 1 shows two conventional field shapes. The meninges and dural extensions are adequately covered, but in both cases there is a risk that the cribriform plate is partially shielded because of the need to limit the dose to the lens.

Figure 2 shows the close relationship of the orbital margin and the cribriform plate. The field centre was placed at the orbital margin so that the lenses were opposed, thus making it easier to avoid underdosage of the cribriform plate. Computed tomograms of the same

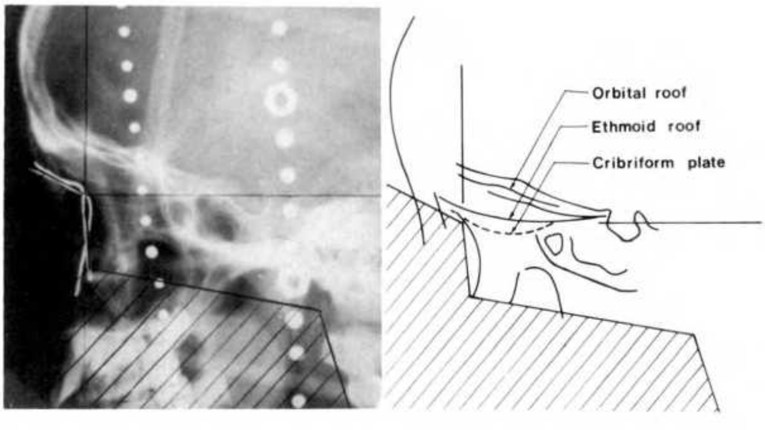

Fig. 2.

Simulator film of a 7-year-old child showing the radiological anatomy of the orbit. In this case the lenses could be shielded without protecting the cribriform plate.

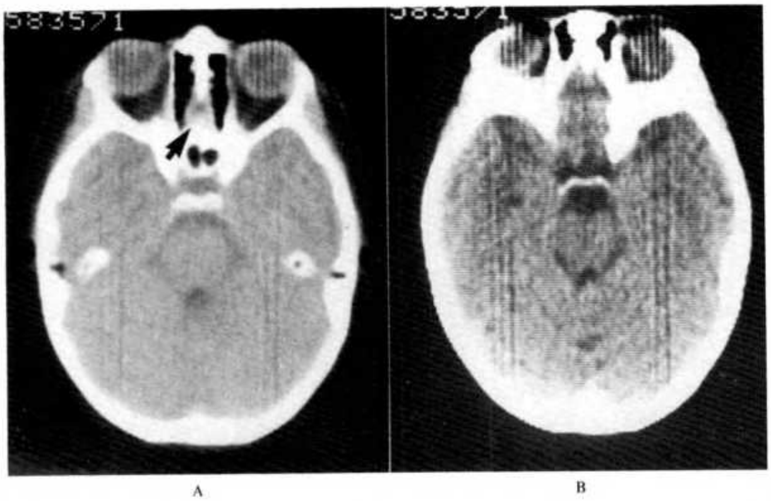

FIG. 3.

(A) Computed tomogram through the central plane of the field shown in Fig. 2, confirming the position of the cribriform plate (arrow). (B) The tissues of the anterior fossa appear in the cut 5 mm superior and the lenses appear in that 5 mm inferior (not shown).

patient confirm the close relationship of the cribriform plate to the proposed orbital shielding (Fig. 3). Dose distributions calculated using this information show that, in this case, lateral fields alone will give an adequate dose to the cribriform plate (Fig. 4A). However, it does lie close to the field edge and in most children and many adults the addition of an anterior electron field will be necessary: it certainly provides a greater margin of safety (Fig. 4B). The precise dose distribution varies in different planes and will be influenced by the air cavities and bones through which the electron beam passes; calculation of the exact dose is not yet available on a routine basis. Nevertheless, because electrons have a limited range in tissue, the dose to the hypothalamus, pituitary and brain-stem will not be significantly increased. Above the eye-shields a small part of the brain which is treated by all three fields will receive a dose of about 180% of that prescribed. The area of high dose will be small and probably acceptable in the treatment of leukaemia, but for medulloblastoma the use of higher whole-brain doses dictates a more cautious approach. If a

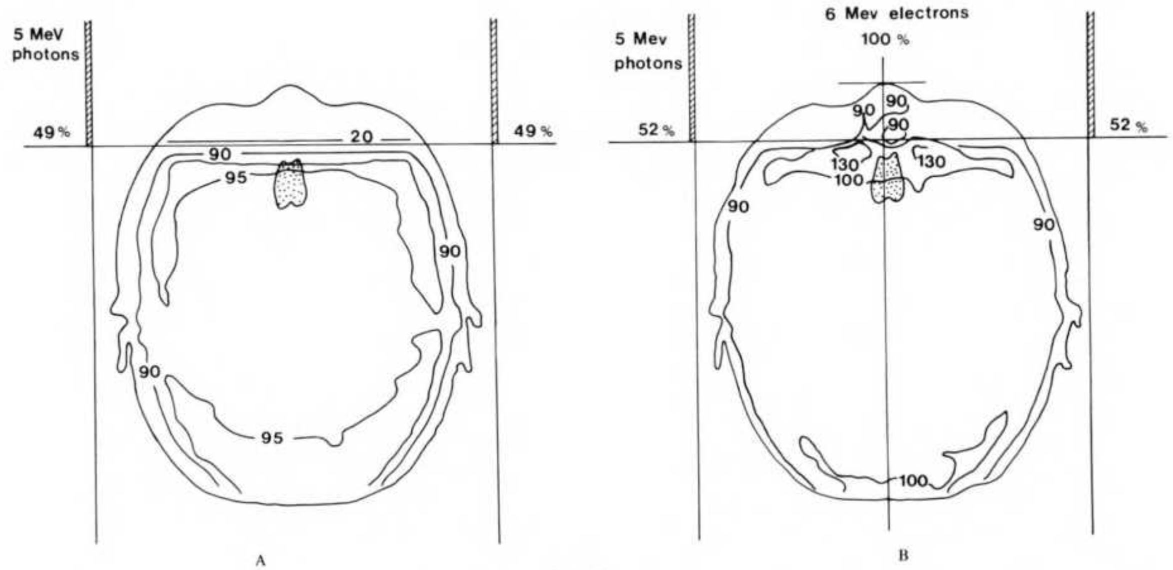

FIG. 4.

(A) Dose distribution calculated using data obtained from CT (Fig. 3). The cribriform plate (shaded) falls within the high-dose region, but lies near its edge so that an error of a few millimetres would alter the dose dramatically. (B) The addition of an anterior electron beam ensures that the cribriform plate receives the full dose prescribed to the brain. This results in an unavoidable increase in dose to adjacent parts of the brain, but the dose to the lens will be almost unchanged.

homogeneous dose distribution is otherwise impossible, the addition of an electron field may provide the best compromise.

MODIFIED TECHNIQUE OF CRANIAL IRRADIATION

The patient lies supine in an anterior head cast. The centre of the field is located by marking the bony margin of the orbit and the position of the outer canthus on the patient before fitting the cast (Fig. 5). In an adult these marks will allow adequate clearance for the lens, whose posterior pole lies about 8 mm behind the cornea. In children it is important to ensure that the field edge falls at least 15 mm behind the cornea (Hancock, 1986), because there is no necessity to irradiate the anterior half of the globe. The skin marks are then reproduced on the shell and lead wire is placed over them so that they can be visualised on the planning radiograph (Fig. 2). If markers are placed directly on the patient they will be displaced by a tight-fitting cast. The simulator is then set up on one outer canthus and the gantry and couch are rotated until the markers are opposed, indicating that the central axis is passing just behind the lenses.

In adults it is then necessary to ensure that the cranium can be encompassed using the field centre chosen. The maximum field size available may dictate that the centre is moved posteriorly 1 or 2 cm. The centres of the fields are then marked on both sides of the shell. A single simulator radiograph is then taken (100 cm isocentric) and used to design both lead shielding blocks. As the beam is centred on the orbital margin the edge will be sharp and will not diverge towards the contralateral eye (Fig. 4A). The posterior part of the globe is included, together with the temporal lobe (1 cm margin at least). The shield includes the facial canal generously and allows a 1 cm margin anterior to the spinal canal. There is no shielding in the region of the posterior part of the neck. Asymmetric jaws are used to define the inferior border; if this facility is not available then additional lead shielding is required.

The first treatment is supervised by the radiotherapist. The position of the eye-blocks is checked, as an error of a few millimetres will drastically alter the lens dose. Check radiographs of the final set-up of both fields are taken and lens doses are estimated using lithium fluoride placed in the inner canthus.

The necessity for an anterior electron field will be decided using the initial simulator radiograph. The electron field measures 3 cm × 3 cm and is centred between the eyes at the level of the cribriform plate, as determined from the simulator radiograph. The electron energy is chosen so that the 50% isodoses of this field and that of the photon fields match in the plane of the cribriform plate, resulting in homogeneous irradiation (Fig. 4B).

Figure 6A shows a simulator radiograph of the adult illustrated in Fig. 5. There is a considerable margin of clearance below the cribriform plate and lateral fields alone were considered adequate. Figure 6B shows a simulator radiograph of a 2-year-old in whom the cribriform plate lies behind the planned minimal orbital shielding, despite using the same anatomical landmarks; an anterior electron field was added during treatment.

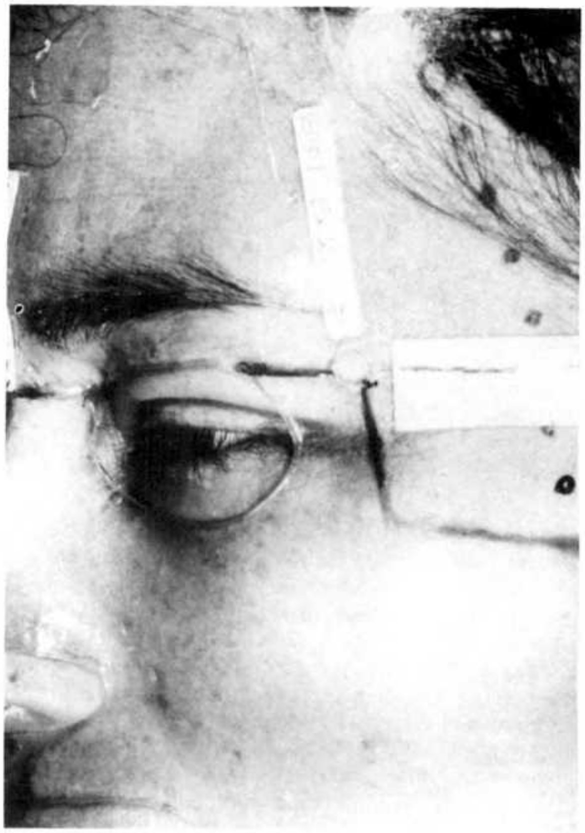

FIG. 5.

Patient in cast, illustrating surface landmarks used to define the orbital shielding. Superiorly the field passes below the orbital ridge and allows protection of the lens. In a co-operative patient the lens can be rotated away from the beam edge if they can be relied on to look downwards. Posteriorly the beam must pass at least 15 mm behind the cornea to avoid the lens, and in adults this point usually coincides with the bony margin of the orbit.

DISCUSSION

In a radiological survey of 5000 American children, the cribriform plate was usually projected over the upper third of the orbit, and was particularly close to the lens in younger children (Broadbent et al, 1975). Nevertheless, it seems that radiotherapists have not been convinced of the importance of restricting orbital shielding. In one multicentre study excessive shielding beyond that specified in the protocol was applied in 35% of cases (Reinstein et al, 1982).

The geometrical problem posed by lens shielding has been recognised before and attempts to sharpen the

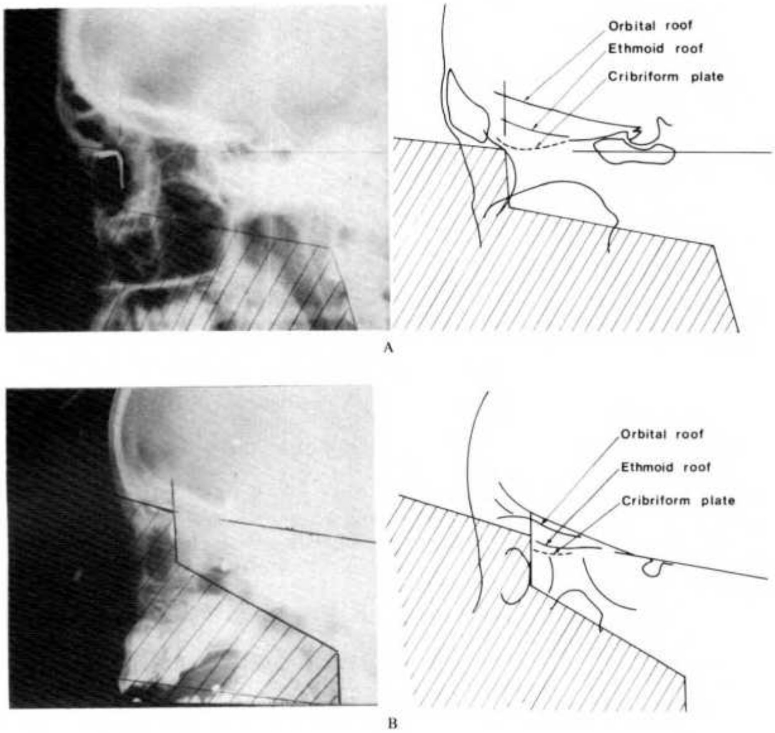

FIG. 6.

(A) Orbital shielding used in the adult patient shown in Fig. 5. The cribriform plate is adequately covered. (B) Orbital shielding used in a 2-year-old child. Adequate lens shielding results in underdose of a large part of the anterior fossa. An anterior electron field was added.

beam edge adjacent to the orbit to overcome the difficulty have been described. Kline et al (1979) advocated altering the entry angle of the lateral fields, but Pla et al (1981) showed that half-axis blocking was a more efficient technique for reducing beam divergence. The fact that such techniques do not provide a solution for all patients was recognised by Hardy et al (1978) and by Jereb et al (1981, 1984), who both suggested the use of anterior electron fields as advocated here.

The risk of underdose to the meninges in the region of the cribriform plate in the treatment of leukaemia has been discussed previously by Jenkins (1979). He commented that there were no data to indicate that this decreased the effectiveness of cranial irradiation. This is because there has been no clinical trial to test the hypothesis. At best, the modification of radiotherapy technique proposed here might be expected to decrease the overall CNS relapse rate from 10% to 2%. To stand a 90% chance of detecting this large difference at the 5% level, 400 cases would be required (Freedman, 1982).

Anecdotal evidence that the dose to the cribriform plate may be important can be derived from a series of patients treated at the Sidney Farber Cancer Center, Boston. The radiation technique used there employed very limited lens protection (Dritschilo et al, 1976) and a very low incidence of CNS relapse of about 3% overall was reported (Green et al, 1980). By contrast, much higher relapse rates of up to 12% have been reported in multicentre studies in which the fields used were determined by the individual radiotherapist (Nesbit et al, 1981): review of the fields and dose-fractionation schemes used did not reveal any significant trends (Littman et al, 1979; Nesbit et al, 1981a, b), but very large numbers of patients would have been required to demonstrate such subgroup differences.

Evidence suggesting that X-ray dose may be critically important in the eradication of meningeal leukaemia can be obtained from a retrospective comparison of two studies in which the dose of cranial irradiation was reduced from 24 Gy to 18 Gy. There was no significant alteration in either CNS relapse rate or survival (Nesbit et al, 1981b). However, the lower X-ray dose was associated with a doubling in the CNS relapse rate in high-risk cases (32% vs 12%), although because of the small numbers involved the difference was not significant ($p = 0.45$).

The cribriform plate may represent a remaining critical area of inadvertent underdose. This problem can be eliminated by careful treatment planning and by checking the actual fields treated using beam films. In most children and many adults the addition of an anterior electron field will be necessary to ensure homogeneous irradiation. The improved dose distribution which results might permit prevention of meningeal relapse with a lower whole-brain dose, and hence fewer neuropsychological sequelae. This hypothesis could be tested in a clinical trial in which the dose of cranial irradiation was further reduced.

ACKNOWLEDGMENTS

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Book review

Polypoid Disease of the Colon Emphasis on radiologic evaluation Ed by David J. Ott and Wallace C Wu, pp. xiii+202, 1986 (Urban & Schwarzenberg, Baltimore, Munich), £42.00.
ISBN 0-8067-1401-8 (Baltimore)
3-541-71401-8 (Munich)

According to the preface, this book was written in response to the stimulus provided by the increasing problem of colorectal cancer in the Western world. The main thrust of it therefore relates to the detection of polyps and cancer by barium enema and these chapters are supplemented by ones on pathology, endoscopy and surgery. Despite its title, it is not a narrow discourse on the polyp/carcinoma sequence and it ranges freely over many aspects of colonic disease. Indeed, as far as the radiology is concerned, diverse pathologies such as endometriosis and appendix abscesses are demonstrated, as is any lesion causing a defect in the barium column These would not be considered polypoid in the traditional sense of the word.

The book opens with a chapter on the pathology of colonic polyps, which is written in a lucid style; all the various types of polyps are considered, including discussion of the adenoma–carcinoma sequence. This is followed by the radiological chapters, which occupy about half the book. These include sections on preparation of the patient, conducting the examination, interpretation and pitfalls The last named is well covered in a chapter entitled "Radiographic Efficiency", which details many of the causes of erroneous reporting. As with many American books on colonic examination, single-contrast barium enemas appear first in the discussion and according to the authors this technique is indicated in about 50% of patients referred for barium enema. This I feel would be a high figure by British standards, and I note that the majority of illustrations are of the double-contrast technique.

From the point of view of Fellowship candidates there is a very useful chapter at the end on polyposis syndromes, a topic dear to the heart of those setting multiple-choice questions in the final Fellowship.

The radiological chapters are complemented by two on endoscopy which I thought gave a very fair summary of the advantages and problems of colonoscopy.

My only reservation about this well illustrated and comprehensive book relates to its potential market. If the authors are looking to the radiologist in training then I would imagine that its scope is too limited. For example, for only £8 more, he or she could buy *Atlas of Colon and Rectum* by Altaras, which is considerably larger and covers the full range of colonic disease If on the other hand they are looking to the more specialised post-Fellowship market, then they have succeeded admirably, and as such the book deserves to be on departmental library shelves

A. FREEMAN

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Brachytherapy of tumour recurrences in the region of the pharynx and oral cavity by means of a remote-controlled afterloading technique

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ABSTRACT

In the period 1981–86, 22 patients with local inoperable tumour recurrences in the mouth and pharynx area had endocavitary contact therapy using a remote-controlled afterloading system at the Radiotherapy Centre of the University of Heidelberg. All patients had had previous surgery and external-beam radiation; some had also received chemotherapy. The technique is described and preliminary results are discussed.

Today, remote-controlled afterloading equipment is available, by which the correct application of radionuclides is possible in respect of both location and time. Feine and Koburg (1968) and Alth (1978) have already mentioned the use of such remote-controlled afterloading techniques in the region of the pharynx and larynx. In this paper we describe, with some preliminary results, a specially developed technique (Bauer et al, 1984) which we used from 1981 to 1986 to treat patients with tumour recurrences. The problems of treatment planning with such brachytherapy have been discussed by Notley et al, (1982) and Schlegel et al (1982).

PATIENTS AND METHODS

Endocavitary therapy in the mouth and pharynx area must fit the tumour site and the patient's anatomy; that means it must be individually performed. To meet these requirements, we need equipment with a great variability in the available sources and source probes flexible enough to fit each patient (Bauer et al, 1984). We have used the Selectron machine (Nucletron), which has six treatment channels that can be charged with active and inactive pellets. Caesium 137 is used for the pellets, the activity of each of which is 740 MBq (20 mCi). Polyethylene probes are used which may be bent under hot air so that quite sharp curves are possible. Special attention has to be paid, however, to preserving the lumen and the use of a spiral metal insert is therefore necessary.

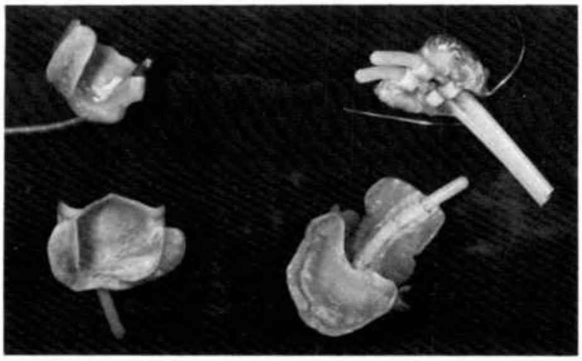

FIG. 1.

Special forms of applicator dentures designed in co-operation with the dental clinic.

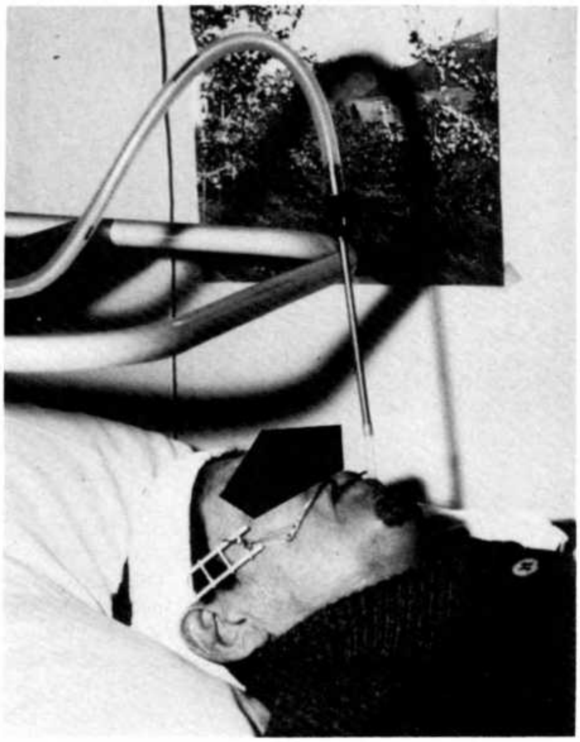

FIG. 2.

Patient under endocavitary contact therapy showing fastening of the applicator denture by rubber flaps to a head-cap and the pneumatic transport tube of the caesium-137 source.

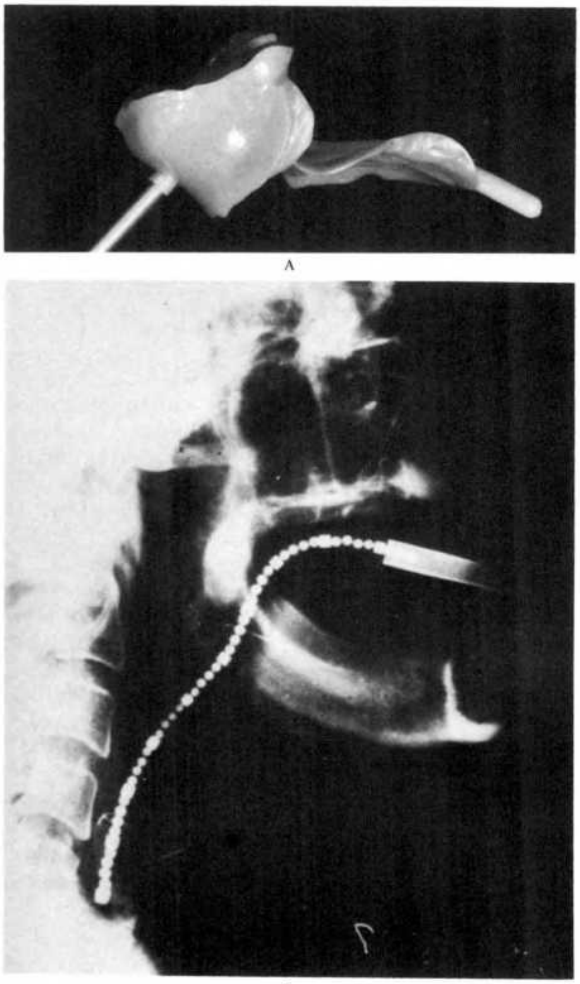

FIG. 3.
(A) Specially made applicator denture with guide splint for irradiation of a tumour recurrence in the region of the hypopharynx. (B) Lateral control radiograph of the fixed applicator denture in (A), with dummy sources, showing that the intracavitary contact therapy will reach even unfavourably located tumours.

Applicator dentures

In co-operation with the Dental Clinic, Heidelberg, we have designed a denture in which the probes are positioned (Fig. 1) for each patient. This guarantees that the sources are placed close to the tumour and that the location of the probe is always reproducible.

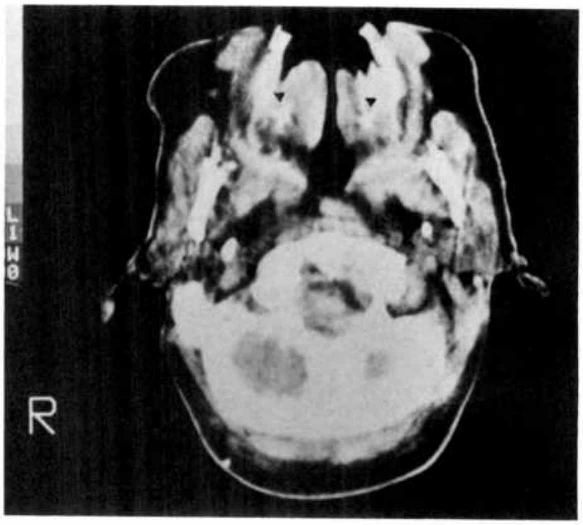

FIG. 4.
A CT scan showing applicator denture. The aluminium reference points, implanted in the applicator denture, can be seen in spite of small artefacts (arrows).

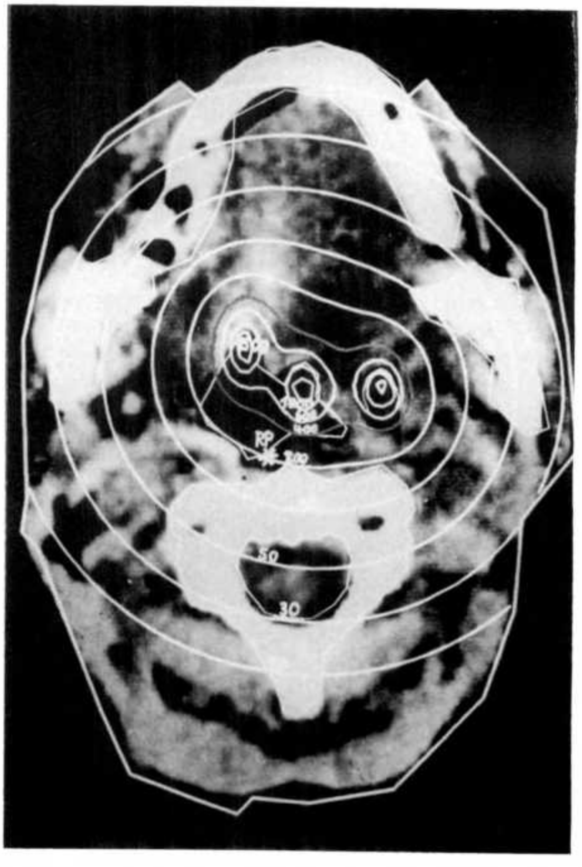

FIG. 5.
A CT scan in the horizontal plane showing tumour recurrence at the base of the tongue. The three applicator probes can be seen as slight impressions. The isodoses show dose rates in cGy h^{-1}. The dose rate in the reference point (RP*) is 2.5 Gy h^{-1}. The target volume is shown by the darker line (400 cGy h^{-1} isodose).

TABLE I

DETAILS OF PATIENTS AND RESULTS

Case	Age (years)	Primary site of tumour	Dose (Gy)	Fractions per week	Total no. of treatments	Response	Duration of the response (March 1986) (months)
1	57	hypopharynx	71	2	8	PR	22
2	58	tonsil	46	3	6	PR	8*
3	63	hypopharynx	60	3	7	TR	25*
4	51	hypopharynx	53	2	7	NC	6
5	63	epipharynx	52	2	6	PR	44*
6	47	mouth	63	3	7	NC	13
7	50	hypopharynx	59	3	6	PR	5*
8	61	oropharynx	56	3	7	PR	23
9	48	tonsil	67	3	8	NC	14
10	47	tonsil	75	3	9	TR	13*
11	49	mouth	64	2	8	PR	17
12	56	hypopharynx	49	3	6	NC	10
13	41	epipharynx	48	3	7	PR	16
14	61	hypopharynx	70	2	9	NC	11
15	52	mouth	53	3	8	NC	9
16	56	hypopharynx	66	3	7	TR	21*
17	46	hypopharynx	51	2	6	PR	14
18	56	tonsil	73	3	8	PR	13
19	63	hypopharynx	59	2	6	PR	7
20	51	oropharynx	64	3	7	TR	30*
21	44	tonsil	54	3	7	NC	11
22	69	mouth	62	2	8	PR	26

PR = partial remission, TR = total remission, NC = no change.
* Then still in partial/total remission

The applicator dentures are fastened to rubber flaps on a head-cap (Fig. 2). For the biteblock dentures, biting is sufficient. In the pharynx region the fastening is more difficult because of the regurgitation reflex. By superficial anaesthesia this reflex can be more or less eliminated and in the case of repeated treatment we have observed a certain tolerance developing in patients. After superficial anaesthesia all patients tolerated treatments of up to 2 h, even in the pharynx region. (Figure 3A shows an applicator denture for irradiation of a tumour recurrence in the region of the hypopharynx. Figure 3B is a lateral control picture.)

Irradiation scheme

Before an irradiation scheme is planned for the region of the mouth and pharynx, the localisation of the applicator probes in the three-dimensional volume by stereo and orthogonal X radiography is necessary Using three reference points in the applicator denture (aluminium balls, diameter 3 mm) the source co-ordinates can be transmitted from the X-ray system to a CT scan. Figures 4 and 5 show the development of such an irradiation scheme. A few artefacts are tolerable. As the applicator probes are shown in the CT scan we have an additional control of their position.

Dosage and fractionation

When planning the total dose to be given in this type of radiotherapy for tumours in the mouth and pharynx, the previous management by surgery, radiotherapy and chemotherapy, as well as the local findings and the likely tolerance of the patient, must be considered. From the beginning of treatment, close co-operation between surgeon, radiotherapist and the patient is very important. When the reference isodose is taken at a depth of 10 mm, the dose rate is in the range 2.5–3.0 Gy h^{-1}; the dose at the surface is limited under these circumstances to 10–15 Gy h^{-1}. Treatment is given two to three times a week to a maximum dose of 10 Gy on each occasion in approximately 1 h. Total dose to the target volume is about 75 Gy.

Patients

Between 1981 and 1986, 22 patients with recurrences of a squamous-cell carcinoma in the region of the hypopharynx and mouth were treated. All these patients had previously undergone surgery as well as irradiation. The dosage of the external-beam irradiation (^{60}Co) was 60–66 Gy. Some of these patients had been treated additionally by pre-operative combination chemotherapy.

RESULTS

The results are given in Table I. We observed total remission in four patients, a partial remission in 11 patients and no change in seven patients. A side-effect in one patient was temporary swelling of the tongue. We did not observe any significant side-effects such as extensive necroses or osteoradionecroses. A high percentage of such side-effects has been reported previously (Fletcher, 1980).

DISCUSSION

The therapy presented here, *i.e.* contact therapy by remote-controlled afterloading probes, presents itself as a suitable therapy for tumour recurrences in the region of mouth and pharynx. By using applicator dentures and remote-controlled afterloading equipment with a good selection of sources, endocavitary contact therapy can be adapted to the anatomy and tumour site of each patient. By this technique we have treated 22 patients suffering from tumour recurrences in the mouth and pharynx. In cases of tumour size of less than 1 cm we observed in all patients a good local decrease in the extent of the tumour and significantly less pain. In cases with tumours of more than 1 cm, interstitial therapy would probably gain better results. Serious side-effects such as extensive necroses or osteoradionecroses have not been observed up to now. We attribute these results to the individual patient planning and to the low dose rate combined with the fractionation of the treatment (Liversage, 1969; Bauer et al, 1987).

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Geometry adopted by Manchester radium applicators and Selectron afterloading applicators in intracavitary treatment for carcinoma cervix uteri

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ABSTRACT

Twenty-eight patients with early-stage carcinoma of the uterine cervix were treated using one standard Manchester radium application and one afterloading Selectron application. In each case, radiographs were analysed to determine differences in geometry of applicators relative to each other, or to the bony pelvis. During the Selectron treatment the applicators lay significantly more anterior in the pelvis, with a reduced angulation between the axes of the uterus and the vagina. The separation between the ovoids was increased. An identical analysis of 25 patients who had received two radium applications showed that the uterine tube lay significantly more anterior in the pelvis during the second application. Reasons for these differences and their possible clinical importance in terms of increased dose rate to critical tissue are discussed.

In the Manchester radium system as applied to treatment of carcinoma of the cervix, the dose rates at a point are standardised using specially designed applicators and appropriate radium loading. The dose-rate calculations assume that the applicators lie in an ideal reference geometry (Wilkinson et al, 1983). When Selectron afterloading equipment (Nucletron Trading BV) was introduced at the Christie Hospital in 1978, a similar assumption was made in order to calculate caesium source patterns which would faithfully reproduce the relative isodose distributions around a standard Manchester radium insertion. However, it was recognised that the idealised reference geometry of applicators was rarely achieved in practice, and that the degree to which the two intracavitary systems approached reference geometry could differ.

Following the introduction of the Selectron afterloading system, a study was set up to investigate treatment of early-stage carcinoma of the cervix. Patients were treated by intracavitary radiation alone, using one radium application and one Selectron application. The prime aim of this study (radium/Selectron group) was to assess any change in short-term morbidity and cancer control related to an increased dose rate from the Selectron application, but this group of patients also afforded an ideal opportunity to evaluate any difference in geometry adopted by the two treatment methods.

It was appreciated that differences in applicator geometry between the first and second insertion could occur in patients treated with two standard Manchester radium applications. A group of patients (radium/radium group) with early-stage disease treated at the same time as the radium/Selectron group were, therefore, analysed in an identical way.

PATIENTS AND METHODS

Thirty patients were entered into the radium/Selectron study. Two patients were excluded from the analysis because check radiographs of intracavitary insertions were missing. Of the 28 patients analysed, 21 had Stage 1 disease and seven had Stage 2A.

The standard applicators and radium loading used in the Manchester intracavitary system have been described in detail elsewhere (Cole & Hunter, 1985). Selectron equivalents were available based on the design of standard Manchester applicators. The distal section of the Selectron intrauterine tube curved, gradually, over 40°. Intrauterine length was determined using a flange located by a spring in grooves on the tube. All applicators were inserted with the patient in the lithotomy position.

For each patient, the relative positions of the two intracavitary insertions were calculated using antero-posterior and lateral radiographs taken immediately after the procedure. Four points of interest were chosen, as shown in Figs 1 and 2: Point P is at the tip of the intrauterine tube; Point Q is at the centre of the flange at the cervical os; and Points R and S are at the centres of the right and left ovoids, respectively. The position of each point within the bony pelvis was defined by using three co-ordinates: the distance left (positive) or right (negative) of the median sagittal plane on the antero-posterior radiograph (x co-ordinate in Fig 1); the distance above (positive) or below (negative) a transverse axial plane through the sacral promontory on the lateral radiograph (y co-ordinate in Fig. 2); and the distance anterior (negative) or posterior (positive) to a coronal plane through the sacral promontory (z co-ordinate in Fig. 2). All measurements

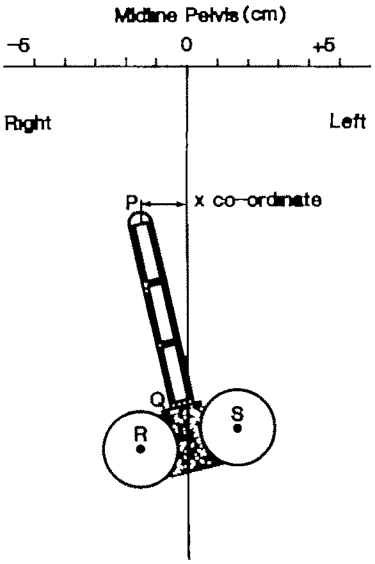

FIG 1.
Diagrammatic representation of Points P, Q, R and S as seen on the antero-posterior radiograph.

were made in cm and corrected to allow for magnification on the radiographs. The Wilcoxon matched-pairs sign test was used to detect any overall significant difference between the positions of Points P, Q, R and S during radium and Selectron applications.

Twenty-five patients were analysed in the radium/radium group. For each patient, applicator sizes and arrangements were the same during both applications. Again the analysis was carried out as described above.

RESULTS

Radium/Selectron group

In 17 patients (61%), radium and Selectron insertions matched in terms of applicator size and geometric arrangement. For this group, the overall differences between co-ordinates for radium and Selectron insertions are given in Table I In summary, substituting the Selectron equivalents for the radium applicators resulted in the following changes:

(a) the tip of the uterine tube was lying more anterior in the pelvis (median difference 11 mm);
(b) the cervix was lying more caudal in the pelvis (median difference 10 mm);
(c) the cervix was lying more anterior in the pelvis (median difference 18 mm);
(d) the ovoids were lying more anterior in the pelvis (median difference 10 mm); and
(e) the separation between the ovoids was increased (median difference 9 mm).

TABLE I

OVERALL COMPARISON OF CO-ORDINATES FOR POINTS P, Q, R AND S IN 17 PATIENTS WITH "MATCHED" RADIUM (RA) AND SELECTRON (SE) INSERTIONS

	Median difference (Ra − Se co-ordinate values) (range)		
	x co-ordinate	y co-ordinate	z co-ordinate
P	NS	NS	Ra > Se: $p < 0.001$ 11 mm (−8 to +54)
Q	NS	Ra > Se. $p < 0.006$ 10 mm (−12 to +43)	Ra > Se: $p < 0.001$ 18 mm (−6 to +38)
R	Ra > Se: $p < 0.002$ 4 mm (−4 to +29)	NS	Ra > Se: $p < 0.007$ 7 mm (−7 to +23)
S	Ra < Se: $p < 0.010$ −5 mm (−14 to +10)	NS	Ra > Se: $p < 0.002$ 12 mm (−8 to +26)

NS = not significant

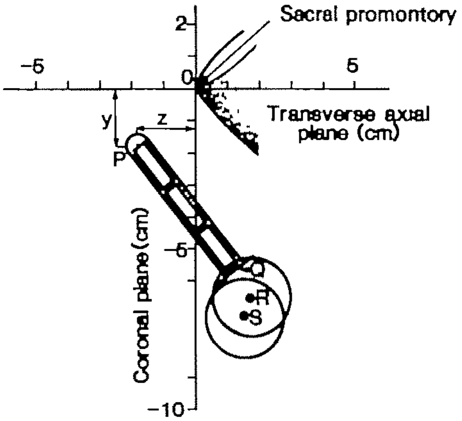

FIG 2.
Diagrammatic representation of Points P, Q, R and S as seen on the lateral radiograph

Typical changes in anterior–posterior positioning are illustrated in Fig. 3 where the displacements shown are the median differences mentioned in items (a) to (d) above.

In the remaining 11 patients (39%): (a) the Selectron intrauterine applicator was 2 cm longer than the radium applicator in four cases (14%) and (b) the radium ovoids were one size larger than Selectron ovoids in five cases (18%) and one size smaller in two cases (7%). Initial small radium ovoids in tandem were substituted by small Selectron ovoids in parallel during the subsequent insertion in two cases (7%). (Two patients fell into both categories (a) and (b) above.)

Radium/radium group

The results of the analysis of the radium/radium group are given in Table II. In summary, during the second radium application the following changes were observed

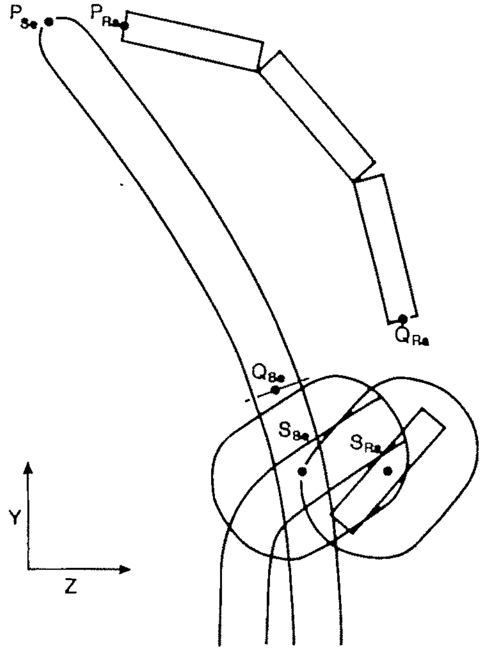

FIG. 3.

Diagrammatic representation of main differences in geometry between radium (Ra) and Selectron (Se) insertions.

(a) The tip of the uterine tube lay more anterior in the pelvis (median difference 6 mm).

(b) The cervix lay more anterior in the pelvis (median difference 4 mm).

Both these differences were in the same direction, but not as marked, as those observed in the radium/Selectron group. There was also an apparent anterior displacement of the ovoids between the two insertions, again in the same direction as observed in the radium/Selectron group, but the figures were not statistically significant.

TABLE II

RADIUM/RADIUM GROUP OVERALL COMPARISON OF CO-ORDINATES FOR POINTS P, Q, R AND S IN 25 PATIENTS WITH "MATCHED" RADIUM APPLICATORS

	Median difference (Ra 2–Ra 1 co-ordinate values) (range)		
	x co-ordinate	y co-ordinate	z co-ordinate
P	NS	NS	Ra 1 > Ra 2: $p < 0\,013$ 6 mm (−28 to +20)
Q	NS	NS	Ra 1 > Ra 2: $p < 0.028$ 4 mm (−34 to +18)
R	NS	NS	NS
S	NS	NS	NS

NS = not significant.

DISCUSSION

This study demonstrates that, superposed on the random variations in applicator positions, there are certain systematic differences which occur between two intracavitary insertions spaced 1 week apart. At first sight, in spite of their statistical significance, none of the differences seem very great. It must, however, be remembered that the dose gradients around the applicators are very steep, and small alterations in position of the applicators relative to pelvic organs can have a marked effect on the dose received by those organs. How clinically significant this is must be open to some conjecture, as precise control of applicator position is not possible and in any group of patients there must be a wide range of doses to these organs.

Changes in position of the uterine tube

The radium/radium study demonstrated that during the second insertion the uterine tube tends to be located more anteriorly in the pelvis The reason for this change is not obvious, but technically the second insertion may be influenced by the effective prolonged dilation of the first insertion or some early primary tumour regression. A similar, but more marked change was observed in the radium/Selectron group. In addition, the cervix appeared to occupy a more caudal position during the Selectron insertion, where the long axis of the uterus has to conform to the fixed angulation of the intrauterine tube. This reduces the probability of vaginal packing pushing the whole applicator set cranially. The flexibility of the radium applicator, however, will allow the normally anteverted uterus to be treated in its natural position, and packing the posterior fornix may increase further angulation between the uterus and vagina.

Although the applicators do tend to be located differently within the pelvis on the second insertion, it is unlikely that this will have any major effect on the dose distribution in the uterus and upper vagina themselves as these organs will tend to move with the applicators In moving forward in the pelvis, however, the applicators are moving towards the bladder, ureters and urethra, and, in patients with a long vagina, towards small-bowel loops that can lie above the empty bladder in the anterior pelvis. Such a movement will also tend to increase the distance to the anterior rectal wall and the sigmoid colon in the posterior pelvis. It cannot be assumed that all these different tissues will move together with the applicators, but neither can it be assumed that their position will be unrelated to the position of the gynaecological organs. There are natural connections between the upper vagina, bladder base, urethra, and rectum. In addition, there are considerable variations in individual anatomy aggravated by restrictions on movements of tissues relative to each other by previous inflammation, surgery, or disease infiltration.

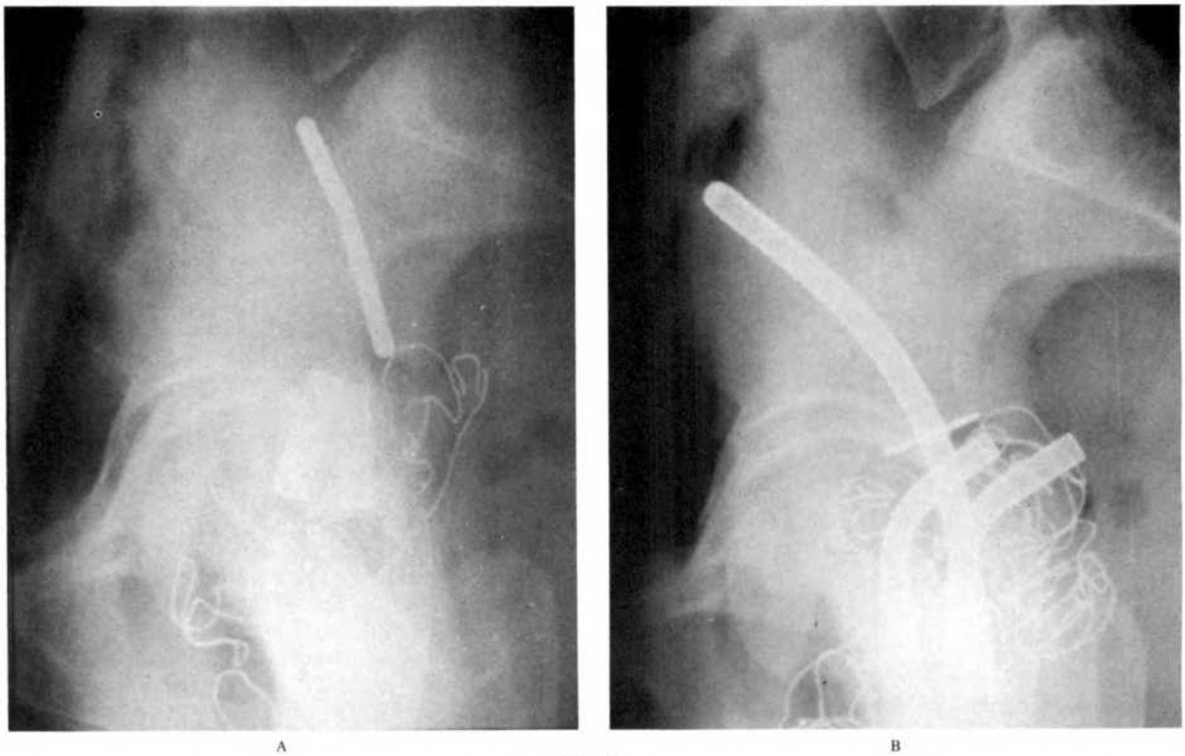

FIG. 4.

Lateral radiographs of pelvis illustrating (A) standard radium insertion with minimal angulation between uterine and vaginal axes (first intracavitary treatment) and (B) Selectron applicator bringing uterus anteriorly out of the sacral hollow (second intracavitary treatment).

A direct comparison of doses to these organs was not possible as part of this study, as identical soft-tissue points cannot be identified in each insertion.

The fixed angulation of the Selectron intrauterine applicator can be of benefit in treating certain patients with a mobile uterus. Two insertions for such a patient are shown in Fig. 4. The minimal angulation between uterus and vagina during the radium insertion is converted to marked anteversion during the Selectron insertion. This represents a major change in dose distributions in organs outside the uterus and, in particular, the danger of over-irradiation of the sigmoid colon in the hollow of the sacrum is avoided.

Changes in position of the ovoids

In the radium/radium group there was no significant difference in ovoid position relative to the bony pelvis from one insertion to the next, but, as noted above, the intrauterine tube tended to be further forward on the second occasion. This would appear to imply that the ovoids were not positioned directly against the cervix. However, it should be noted that in the radium system the ovoids may rotate so that their long axis is no longer at right angles to the intrauterine tube. This will effectively increase the distance between Point Q and Points R and S without necessarily implying a poor insertion.

In the radium/Selectron group the Selectron ovoids tended to be (a) more anteriorly placed with respect to the bone structure, but more posteriorly placed with respect to the lower end of the intrauterine tube, and (b) more widely separated. In the Selectron application the ovoid position relative to the intrauterine tube is fixed by clamping and will not be altered by packing of the posterior fornix. Posterior packing will instead tend to push the whole applicator set forward. The wider separation is, in part, required to accommodate the intervening central tube (6 mm external diameter). However, there is also a scissor action on the ovoid carriers which will allow the ovoids to be pushed and held more laterally in the upper vagina than is possible with the unconnected radium ovoids. Stretching of vaginal vault tissue may possibly reduce vascular perfusion and predispose to subsequent vault morbidity.

CONCLUSION

When the Selectrons were introduced into the Christie Hospital it was anticipated that the increase in dose rate by a factor of three might affect the clinical results, particularly with regard to the incidence and pattern of morbidity (Wilkinson et al, 1980). Clinical trials were inaugurated in order to investigate the dose-rate effect and considerable effort was directed towards isolating dose rate as the only significant variable. This study has demonstrated a more subtle and unexpected group of systematic geometrical differences which may be significant. In particular, there may be a tendency to increase the risk of vault damage and anterior pelvic tissue injury while correspondingly reducing the risk to posterior pelvic large bowel. In assessing morbidity in patients treated using the Selectron it is important not to ascribe all morbidity to dose-rate effects and to ignore the possibility that some may have been caused by dose distribution changes and geometrical factors.

ACKNOWLEDGMENTS

We would like to thank Mrs V Blair for the statistical analysis.

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Book review

Comprehensive Textbook of Oncology. Ed. by A. R. Moossa, M. C. Robson and S. C. Schimpff, pp. 1307, 1986 (Williams & Wilkins, Baltimore), £129.
ISBN 0683–06149–6

This textbook amply satisfies the current need for an up-to-date multidisciplinary reference manual on oncology and I strongly recommend that all medical libraries should have a copy. It is remarkably comprehensive and although it is inevitably a large and heavy book, the individual topics are covered in a short, concise and clear way, ending with a limited number of core references and recommended readings, albeit mostly from the USA. The whole is an enthusiastic and optimistic overview which wisely avoids unnecessary technicalities. The editing is excellent, as are the illustrations, particularly those in colour which illustrate cutaneous and ocular manifestations of cancer.

The textbook is divided into two sections of which the first, "General Concepts", covers cancer biology, epidemiology and prevention, the full range of diagnostic modalities, the basic principles of cancer therapies and cancer care, and the design of clinical trials. A chapter on the management of cancer pain by Bonica and Benedetto is particularly welcome. This important topic is often omitted from general oncology textbooks. Part two, "Approaches to Specific Neoplasms", deals with the nature and management of tumours, including a separate section on paediatric tumours, divided by organ systems. Again wisely, the authors and editors have largely avoided details of therapeutic debate on optimum treatment but at the same time have indicated where they think potential advances may have a role.

An additional topic, which could usefully be incorporated when this book goes into a second edition, is that of active but palliative treatment by surgery, radiotherapy and chemotherapy in advanced cancer. Many of these interventions (*e.g.* treatment of bone metastases and spinal cord compression) are covered in part two but are difficult to find, and it would be valuable to have them grouped together.

Other than this, it is easy to find information. The postgraduate student of oncology can find succinct details ranging from the cell cycle and tumour markers to the state-of-the-art in adjuvant chemotherapy. For the established oncologist the book provides useful and up-to-date information on newer forms of diagnosis and treatment, and on rare tumours, and even gives us an authoritative account of unorthodox cancer therapies.

Thelma D Bates

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Abdominal computed tomography in teratoma of the testis: its accuracy in Stage I disease and an assessment of the distribution of retroperitoneal lymph-node metastases in other stages of the disease

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ABSTRACT

One hundred and one patients with Stage I teratoma of the testis have had an abdomino-pelvic computed tomography (CT) scan. These patients have been followed up for a minimum of 18 months and only eight patients have relapsed in the abdomen alone. The abdomino-pelvic CT scan has a negative predictive value of 92%. In those shown by CT to have retroperitoneal lymphadenopathy, the distribution of disease correlates closely with that reported in the literature following retroperitoneal lymphadenectomy The CT scan provides information about the amount of tumour present and this influences treatment Computed tomography is the imaging modality of choice for staging patients with teratoma of the testis and invasive techniques do not appear to be justified

Owing to its iterative embryological development, the lymphatic drainage of the testis is to relatively distant nodes in the retroperitoneum. Assessment of these nodes is of vital importance in the management of patients with testicular tumours as they can be the first or only site of metastatic tumour Clinical assessment of retroperitoneal nodes is unsatisfactory as only masses greater than 5 cm in diameter can be reliably palpated, and for many years the only form of radiological assessment, *i.e* deviation of the course of the ureters on an intravenous urogram, was little better. During this period the operation of retroperitoneal-node dissection (retroperitoneal lymphadenectomy) was developed as both a diagnostic and a potentially curative procedure (Patton & Mallis, 1959; Staubitz et al, 1973). This operation was widely adopted in the United States and many other countries but found few advocates in the United Kingdom (Donohoe, 1977). In the UK a different approach was adopted, namely that of assuming that the nodes were involved and offering post-operative abdomino-pelvic radiotherapy as a routine treatment to all patients except those in whom metastatic disease was evident elsewhere (Hope-Stone et al, 1963; Peckham, 1979). Neither of these approaches is without its drawbacks or complications and, with the recognition that many patients will be cured by orchidectomy alone, accurate assessment of the retroperitoneal nodes has assumed greater importance. Although bipedal lymphography has been used for many years to do this (Kinmonth, 1955; Jackson et al, 1964), it is now being replaced by X-ray computed tomography (CT). This paper examines the accuracy of CT in excluding retroperitoneal metastases. The distribution of retroperitoneal metastases in patients with Stage II, III and IV disease has been documented and correlated with reported data from post-mortem studies on retroperitoneal lymphadenectomy

PATIENTS AND METHODS

All patients were scanned on a fourth-generation EMI 7070 scanner Patients were examined in the supine position, 1 cm-thick sections being obtained at 2 cm intervals from the xiphisternum to the pubic symphysis using a 3 s scan time. The bowel was opacified in all patients by giving 250 ml of 5% Gastrografin (Schering AG) by mouth 12 h, 3 h and 0.5 h before the scan. A smooth-muscle relaxant (hyoscine butylbromide 0.5 mg intramuscularly) was given immediately before the scan. Intravenous contrast medium to delineate the ureters and bladder was not used routinely.

All patients had undergone orchidectomy and the histology had been reviewed at the Christie Hospital. Patients were considered to be at Stage I if the clinical examination, chest radiograph, and abdominal and thoracic CT scans were normal and biochemical markers had returned to normal The biochemical markers routinely measured were alpha-fetoprotein (AFP) and human chorionic gonadotrophin (HCG). These patients were followed up in a dedicated clinic and the results of this policy documented (Read et al, 1983).

The criteria for Stage II, III and IV disease are detailed in Table I. The treatment of this group of patients has been documented (Wilkinson, 1985; Read et al, 1986).

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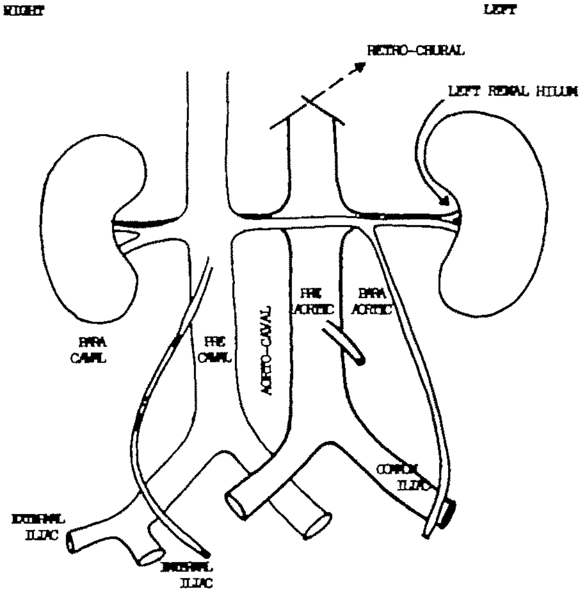

FIG. 1.

Diagrammatic representation of lymph-node areas, after Donohue et al (1982).

TABLE I

STAGING CRITERIA

Stage I
No tumour at the cut end of the spermatic cord
No clinical evidence of residual or metastatic disease
Normal chest radiograph
Normal abdominal and thoracic CT scan
Normal serum markers (AFP, HCG)

Stage IIA
No clinical evidence of residual or metastatic disease
Abdominal CT scan demonstrates lymphadenopathy less than 5 cm in diameter

Stage IIB
Abdominal CT scan demonstrates lymphadenopathy greater than 5 cm in diameter

Stage III
Disease in the mediastinum and/or supraclavicular nodes, with or without disease below the diaphragm

Stage IVA
Lung metastases, less than six in total and none measuring more than 2 cm in diameter

Stage IVB
Lung metastases more extensive than above

Stage IVC
Liver, bone or brain metastases

In the first part of this study the abdominal CT scans of patients with Stage I disease referred between January 1979 and December 1984 were reviewed. In the second part the abdominal CT scans of patients with Stage II, III and IV disease referred between January 1981 and December 1982 were reviewed.

RESULTS

Stage I disease

One hundred and one patients with initial Stage I disease were seen between January 1979 and December 1984. All these patients had an abdominal CT scan available for review. To date, 86 of the 101 patients have shown no evidence of relapse with a follow-up period ranging from 18 months to 6 years. Of the 15 patients who have relapsed, eight have had disease in the abdomen alone detected by a repeat abdominal CT scan and seven have had disease outside the abdomen detected with a normal repeat abdominal CT scan.

Assuming that those patients who relapsed in the abdomen had micrometastases in the lymph nodes at presentation, then there were eight false negative initial scans. The negative predictive value of the CT scan was therefore 92%

Stage II, III and IV disease

Of the 81 patients referred between 1981 and 1982 with clinical Stage II, III or IV disease, 12 patients had had previous treatment and were excluded from the study. Abdominal CT scans of the remaining 69 patients were available for review and, of these, 46 were abnormal. The distribution of lymphadenopathy in this group of patients has been documented using the classification of lymph node groups as described by Donohue et al (1982). This is illustrated in Fig. 1. This classification was used so that comparison could be made with the published data relating to pathological staging. The sites of lymphadenopathy are detailed in order of frequency from left-sided teratoma of the testis in Table II and from right-sided teratoma of the testis in Table III.

The frequency of retroperitoneal nodal involvement following lymphadenectomy reported by Ray et al (1974) and Donohue et al (1982) are detailed in these tables for comparison.

DISCUSSION

There are various methods for detecting metastases within the abdomen from testicular tumours, ranging from surgery, including retroperitoneal lymphadenectomy, through the invasive procedures of lymphography to the non-invasive techniques of ultrasound and CT. Arguments continue in the literature as to which method or methods should be used. The decision as to what to do in individual patients depends on the clinical assessment, the accuracy of imaging techniques and their availability.

The major pathway of spread of testicular tumours is via the lymphatic system. The lymph vessels of the testis commence in two plexi. The superficial plexus is located under the tunica vaginalis, and the deep plexus is in the

TABLE II

SITES OF RETROPERITONEAL SPREAD OF LEFT-SIDED TESTIS TUMOURS

Site	This study ($n = 31$)	Ray et al (1974) ($n = 61$)	Donohue et al (1982) ($n = 42$)
Para-aortic	26 (84%)	60 (99%)	36 (86%)
Renal hilum L	8 (26%)	—	—
Pre-aortic	4 (13%)	10 (16%)	37 (88%)
Common iliac L	4 (13%)	3 (5%)	14 (33%)
Aorto-caval	2 (7%)	10 (16%)	31 (74%)
Pre-caval	2 (7%)	0	1 (2%)
Paracaval	2 (7%)	0	1 (2%)
Internal iliac L	1 (3%)	—	—
Internal iliac R	1 (3%)	—	—
Common iliac R	0	—	2 (3%)
Retrocrural L	1 (3%)	—	19 (45%)
Retrocrural R	1 (3%)	—	10 (24%)
Retro-aortic	1 (3%)	—	—
Spermatic cord L	1 (3%)	—	—
External iliac L	0	1 (2%)	—

TABLE III

SITES OF RETROPERITONEAL SPREAD OF RIGHT-SIDED TESTIS TERATOMAS

Site	This study ($n = 15$)	Ray et al (1974) ($n = 61$)	Donohue et al (1982) ($n = 58$)
Pre-caval	7 (47%)	19 (31%)	43 (74%)
Aorto-caval	7 (47%)	42 (69%)	54 (93%)
Paracaval	4 (27%)	10 (16%)	17 (29%)
Para-aortic	4 (27%)	11 (18%)	6 (10%)
Retrocaval	2 (13%)	—	—
Pre-aortic	1 (7%)	11 (18%)	35 (60%)
Renal hilum R	1 (7%)	—	—
Renal hilum L	0	—	—
Common iliac R	0	10 (16%)	11 (19%)
External iliac R	0	3 (5%)	—
Common iliac L	0	1 (2%)	5 (9%)
Retrocrural L	0	—	13 (22%)
Retrocrural R	0	—	6 (10%)

substance of the testis and epididymis. There are four to eight collecting trunks which ascend in the spermatic cord together with the testicular vessels; these then accompany the testicular vessels as they lie on the psoas major. Classical teaching is that the primary lymph drainage from the left testis is to the renal hilar nodes, accompanying the gonadal vessels which arise from or drain into the artery and vein respectively. Drainage also occurs to the para- and pre-aortic nodes. On the right side the primary drainage is to the paracaval, precaval and aortocaval lymph nodes (Grant, 1958; Warwick & Williams, 1973). Studies in which direct testicular lymphography has been performed demonstrate that lymph from the testis drains to a primary centre, located laterally to the lumbar vertebral body between L1 and L3 on the left side and at L2 on the right side. Lymph then flows cranially and caudally to other nodes around the aorta and inferior vena cava (Chiappa et al, 1966).

Haematogenous spread can occur with metastases to the lungs, liver and brain.

Concerning the detection of lymph-node metastases, various comparisons between surgery and imaging techniques have been reported. Compared with pathological staging from retroperitoneal lymphadenectomy, lymphography, in experienced hands, has an accuracy ranging from 62% to 89% (Kademian & Wirtanen, 1977; Storm et al, 1977) and CT scanning 73–89% (Thomas et al, 1981; Richie et al, 1982). Against these reported accuracies must be weighed the morbidity and occasional mortality from retroperitoneal nodal dissection. Complication rates of 11% (Lindsey & Glenn, 1976) and 12% (Staubitz et al 1974) have been reported. Ejaculatory impotence is common, being reported in 84% of patients by Bracken and Johnson (1976).

Lymphography is an invasive procedure, with recognised morbidity, which requires time and technical expertise to perform. Certain lymph-node groups—the internal iliac chain, upper retroperitoneal and retrocrural nodes and the eschelon nodes—are not opacified, and the limits of tumour may not be delineated because of the failure of contrast to opacify nodes replaced by tumour (Wilkinson & McDonald, 1975). Computed tomography is a non-invasive technique, acceptable to patients and capable of identifying involved nodes outside the lymphographic area, unopacified involved nodes within the lymphographic area and liver metastases. Neither technique can identify micrometastases, which are estimated to occur in up to 17% of patients with Stage I disease (Peckham et al, 1982). The potential advantage of lymphography over CT is in detecting metastases in normal-sized nodes (< 1.5 cm in diameter), but in a series of 225 patients reported by Husband and Grimer (1985) only three patients (1%) had a positive lymphangiogram and a negative CT scan. Computed tomography gave additional information in 23 patients (10%) and seven of these patients had a negative lymphangiogram. Erlichman et al (1981) reported that a combination of lymphography and CT did not significantly improve the diagnostic accuracy of either technique. These two studies show that lymphography does not provide additional information affecting management in a significant number of patients.

The results from this current study in patients with Stage I disease, where CT was used as the only abdomino-pelvic staging investigation, demonstrate that CT is a reliable technique with a negative predictive value of 92%. The patients in this study have been followed up for a minimum of 18 months and published data (Peckham et al, 1982; Read et al, 1983) indicate that the majority of relapses in patients in whom a follow-up policy is adopted will occur within that time. The number and frequency of scans which should be performed after the initial assessment is contentious. Many patients will relapse with raised tumour markers or with metastases which can be recognised on chest radiographs. Repeat CT scans are necessary to detect those patients who relapse with marker-negative disease in the abdomen only. Peckham et al (1982) recommended scanning every 2 months for the first year and every 3 months in the second year of follow-up. This policy results in a large number of negative scans and a workload which is difficult to deal with in CT scanning departments. In our initial study (Read et al, 1983) we did not carry out any CT scans after the initial assessment and, although no patient failed to be salvaged after relapse, we now recommend a second scan at 3–4 months in all patients and, in those patients who are marker-negative pre-operatively, repeat scans at 3–4-month intervals over the first year.

The distribution of retroperitoneal lymphadenopathy identified by CT in this series demonstrates that left-sided testicular teratoma spreads ipsilaterally, in order of frequency, to the para-aortic, left renal hilum, pre-aortic, common iliac and aorto-caval nodes. Contralateral spread is to the pre-caval, paracaval and internal iliac nodes with an equal but low frequency. Retrocrural spread was observed only in the presence of involved retroperitoneal nodes. Right-sided testicular teratoma spread ipsilaterally to the pre-caval, aorto-caval, paracaval and retrocrural nodes. Contralateral spread was to the para-aortic and pre-aortic nodes. Three patients with a right-sided testicular teratoma demonstrated involvement of left-sided nodes without ipsilateral nodal involvement. Contralateral lymphadenopathy without ipsilateral involvement was not seen in those patients with left-sided testicular teratomas.

Ray et al (1974) and Donohue et al (1982) have documented the sites of retroperitoneal nodal metastases from lymphadenectomy specimens (Tables II, III) and the distribution of disease correlates with that identified by CT in this series. Both groups of authors state that it was rare to have contralateral metastases in the absence of ipsilateral metastases and if it occurred it was with a right-sided tumour with left-sided lymphadenopathy. Heiken et al (1984) have also made the same observation and Chiappa et al (1966) had one patient where right-sided testicular lymphography outlined the contralateral para-aortic nodes only The reasons for this cross-over are not fully understood but probably relate to the pattern of valves within the lymphatic vessels. In the light of the work of Chiappa et al (1966) on testicular lymphography, it is interesting that in this series only 26% of left-sided tumours metastasised to the left renal hilum, with the majority metastasising to the para-aortic nodes. It seems unlikely that the primary site of lymph drainage from the left testis is to the renal hilum, as taught classically.

We cannot determine the accuracy of CT in detecting lymph-node metastases at all sites from this study. However, the percentage of patients with intra-abdominal metastases in whom CT did not identify these at any sites is low (8% in this series). These patients may have other evidence of metastatic tumour, such as raised serum AFP or HCG and, if monitored regularly, the disease should be identified, enabling appropriate therapy to be commenced.

The detection of intra-abdominal metastases affects the treatment of a patient who is usually given combination chemotherapy initially. The size of the lymph nodes involved and the presence of liver metastases will affect prognosis and the amount of chemotherapy necessary to obtain complete remission. This information is readily available from the CT scan and it also enables the response to treatment to be monitored. If radiotherapy is to be given for residual bulk disease (Read et al, 1986) then the CT scan will provide for optimal radiotherapy planning.

If CT is used as the only intra-abdominal staging investigation in this group of patients then the areas of likely metastatic spread must be carefully examined. Equivocal scans should be repeated in 6–8 weeks, even if the patient remains well and the serum markers are normal Equivocal findings on the CT scan relating to the contralateral side of the tumour, without evidence of ipsilateral disease, are unlikely to represent metastases but should still be monitored

CONCLUSION

In this series, CT has been reliable in excluding and detecting intra-abdominal metastases. As it is a non-invasive technique which provides information similar or additional to that obtained from invasive techniques, it is the imaging modality of choice in staging testicular tumours With modern treatment regimes and follow-up policies, retroperitoneal lymphadenectomy does not appear to be justified as an alternative staging technique.

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Book reviews

Imaging of Orthopedic Trauma and Surgery. Ed. by T H. Berquist, pp. xiv+799, 1986 (W.B. Saunders Company, Philadelphia), £130.00.
ISBN 0-7216-1102-8

The reporting of trauma radiographs in this country is frequently ignored or delegated to the junior radiologist in the department. This means that complicated injuries to the difficult regions, *e.g.* spine, pelvis and feet, are poorly understood, particularly by senior radiologists. This book will be of considerable value to the radiologist trying to interpret the more complex fractures and dislocations.

The first chapter is on imaging techniques and is written mainly for orthopaedic surgeons. Other chapters on fracture healing, musculo-skeletal infections, stress fractures and interventional techniques would be of value for both radiologists and orthopaedic surgeons. The remaining 11 chapters are concerned with the specific regions of the body and it is these that will be of particular interest to the radiologist. The first few pages of each chapter deal with anatomy and radiographic techniques, and they will be of great help in interpreting plain radiographs and computed tomography (CT) scans The remaining parts of each chapter enter into details of fractures, dislocations, soft-tissue injuries and their complications and treatment.

The text is of a high standard, containing most of the information, both anatomical and radiographic, to enable accurate analysis of images. The references are confined to the most relevant and helpful books and papers, and they are neither too few nor overwhelming

Some inaccuracies are encountered in both the labelling and the legends, *e.g.* in Fig. 3-5A the anterior and posterior tubercles of a cervical vertebra are depicted in reverse, and in Fig. 6-58 the patient is positioned for examination of the lateral not the medial meniscus. A few of the pictures are of poor quality *e.g.* Fig. 4-7 where both the fat-planes and their means of identification can hardly be seen.

The quality of the images is generally of a high standard with the anatomical studies, line diagrams and radiographic images being very relevant to the text and extremely helpful in interpreting one's own films.

This is a book which I can recommend to radiologists and orthopaedic surgeons. I think it is one which would be most appropriate within the X-ray department, immediately available to help in interpretation of plain radiographs and CT scans.

B. J. PRESTON

Computed Tomography in the Evaluation of Trauma, 2nd edit Ed. by Michael P Federle and Michael Brant-Zawadzki, pp. xiv+305, 1986 (Williams & Wilkins, Baltimore), £51.00.
ISBN 0-683-03102-3

Improvements in CT hardware and software have greatly extended the value of CT in the assessment of traumatised patients beyond the confines of the intracranial cavity. This book, now in its second edition, is based on the extensive experience of the authors at the San Francisco General Hospital in this important application of CT.

There are contributions from nine authors with separate chapters devoted to trauma involving the head, face, larynx, spine, chest, abdomen and pelvis. In each anatomical area, the indications for CT and the examination technique are discussed, followed by a description of the types of injury encountered and the resulting CT appearances. The outstanding feature of this book, however, is the large number of high-quality illustrations presented, accounting for almost two-thirds of the entire book Examples of most types of injury described in the text are provided, virtually all produced by modern scanners. The use of high-resolution scanning and multiplanar reformatting techniques are well demonstrated, particularly in relation to maxillofacial and spinal injury.

This is an enjoyable book to read, extensively illustrated and full of practical information. It can be recommended to all radiologists involved in the assessment of injured patients by CT and would be a valuable addition to the bookshelves of CT departments

J. E. GILLESPIE

1987, *The British Journal of Radiology*, 60, 493–495

MAY 1987

Technical notes

Rapid slide reproduction of text and radiographs

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(*Received September 1986*)

Many radiologists give talks and lectures and their subjects require effective illustration, often with both text and radiographs. We have found that hospital photographic services cannot always offer the rapidity, flexibility and accuracy we require and have therefore gained experience in producing slides ourselves

SLIDES OF TEXT

White letters on a blue background

The professional approach to achieving this effect is to use a difficult and expensive diazo technique. This produces brilliant white letters on a blue background. An excellent substitute for this is suggested by Eastman Kodak (1981) in *Making Lecture Slides*, using Vericolor slide film 5072. We have extensive experience with this technique and recommend it. The equipment needed is a 35 mm camera with manual exposure capability, a close-up lens, a cable release, an orange filter (Cokin No. 002) and a copy stand. A macro lens is best but a cheaper screw-on close-up lens attached to the camera's 50 mm lens will suffice. The orange filter gives a mid-blue background. Other filters give different-coloured backgrounds and changing the light source of the copy stand from tungsten to fluorescent gives a different range of colours. The text to be photographed is typed using a carbon ribbon typewriter in the centre of a sheet of white paper. We find that a sans-serif typeface projects best and that a facility for double thickness letters on the typewriter gives outstanding legibility (Fig. 1). A sheet of carbon paper behind the text as it is being typed produces black letters on the back of the page which contribute to the clarity of the letters on the slide. A maximum of six lines of text per slide is recommended but satisfactory slides with more text are feasible if clearly laid out.

Computer-generated typescript is also feasible, as are graphics, but these project well only if the printer uses a daisy-wheel rather than a dot-matrix system (Hunter & Brewer, 1985).

Vericolor slide film 5072 is produced in 100-foot rolls by Kodak. It can be wound onto film cassettes quite easily using a bulk film loader or prepared simply by cutting a length in total darkness and winding it into a cassette. A camera stand is set up with two 60 W tungsten bulbs angled at 45° to the text and about 12 in from it (Fig. 2). It is important to ensure that the text is illuminated evenly and that the room light is of the same intensity during each photographic session. It need not be very dark, just consistently reproducible. Using a simple screw-on close-up lens on the camera's 50 mm lens, and a Cokin No. 002 orange filter, our optimal exposure is 2 s at f4. No film speed needs to be set as this is a wholly manual technique. A cable release prevents camera shake It is advisable to take a test series on the first occasion, changing the exposure by half-stop increments around that suggested to find the best exposure for the circumstances.

The film is developed by the C-41 process used in any of the rapid-development photographic laboratories. Ask for it to be developed but not printed or cut. This is cheap and takes about 15 min. The film can be developed by hand but this is inconvenient. Following

1. Standard sans-serif typeface.

2. **Double thickness typeface.**

3. Multiple-use ribbon, serif typeface.

FIG. 1

Typefaces for slides No 2 is ideal and No. 3 unacceptable on projection.

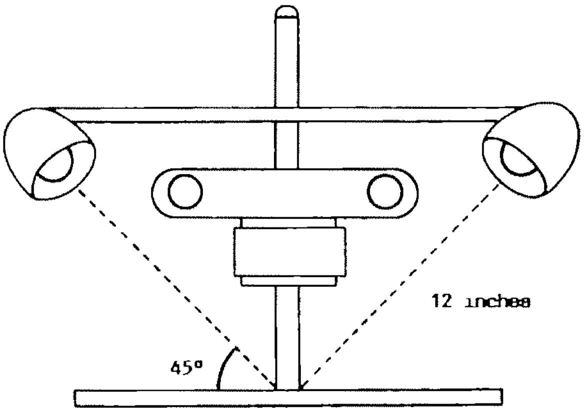

FIG. 2.

Diagram of camera, copy stand and lighting arrangement.

cutting and mounting, it is ready for projection. Until experience is gained at judging the exposure it is advisable to project the slides in the circumstances that they will be used to check legibility. Small changes in the exposure have marked effects on the final contrast and brightness of the slide. The legibility of material on the slide may be judged by reading the slide at arm's length, but overall contrast is best judged with a projector.

Vericolor may be used very successfully to copy diagrams or lists from various sources. Under bright illumination, letters on the other side of the page may show through. This is prevented by putting a black card or an overexposed radiograph behind the item to be copied. Masking of text must be done with white paper or card when using Vericolor.

White letters on a black background

Some people prefer white or coloured letters on a black background. This technique is not difficult but it requires hand processing of the film for best results. No filters are required. Uniform illumination of the text is again important. Kodalith ortho film 6556 Type 3 is used and the text is prepared and photographed as for the Vericolor technique. Our optimum exposure is half a second at f4 with two 60 W tungsten bulbs, 1 foot from the text and set at 45°. The film is available in 100-foot rolls and ought to be processed in Kodalith developer. This is not convenient as the developer is sold in unsuitably large amounts. An acceptable alternative is a single immersion in a 1 in 4 solution of Patterson's Universal Developer for 60 s, followed by fixing and washing. Where manual development is not feasible, we have found that rapid development of this film is possible using an automatic X-ray processor. This method produces a slight increase in apparent film speed of the film, and requires less exposure (for example, we use 0.25 s at f4). In the darkroom the film is taped to a waste radiograph and fed into the processor. In 90 s it is ready to be cut, mounted and coloured if required. Permanent felt pens can be used to highlight words, titles, or the whole text. Yellow is the most effective colour and the letters should be coloured on both sides of the film to obtain good saturation in the projected slide.

Black letters on a white background

This is the least attractive method, but is easy to do. Agfa Dia Direct is the only readily available monochrome slide film. It has an ASA of 32 and is easy to use as it needs no filters. Meter readings of text should ideally be taken from a grey card to avoid overexposure. The film is process-paid and is returned uncut and unmounted in a few days.

We use Kodak Rapid Process copy film mainly for reproducing radiographs, but it reproduces text and drawings well also. It is sold in 36-frame cassettes and in bulk rolls. The film speed is very slow, being about 2000 times slower than colour slide film of 100 ASA. Long exposures are its main disadvantage, and rapid processing via X-ray processors its main advantage. This film is discussed further under reproduction of radiographs.

Colour slide film under tungsten light may be used but a blue filter (Kodak Wratten No. 80B or Cokin No. 021) is needed to produce a white background. Polaroid 35 mm Instant slide film is produced in a 40 ASA black-and-white format and also as a high contrast "lith" film. Either can make acceptable slides of text, but these films share with the others in this section a certain drabness on projection.

We recommend the Vericolor 5072 slide film for reproduction of text, as it is attractive and clear on projection and easy and cheap to produce the slides.

SLIDES OF RADIOGRAPHS

Radiographs are difficult to demonstrate to groups of any size. Rapid reproduction in slide form is required for meetings, lectures and personal collections.

1 Kodak Rapid Process Copy (RPC) slide film is most commonly used for radiograph reproduction It is a slow film, but the exposure time depends also on the f-stop chosen, the intensity of the illuminating system and the density of the radiograph. It varies from several seconds to several minutes. The usual practice is to estimate an exposure from experience, then take a number of exposures around that estimated (bracketing), and hope that one will be suitable. This is wasteful and time-consuming.

A useful method of estimating the correct exposure for a radiograph using RPC film and a camera with an exposure meter has been published (Onitsuka and Matsuura, 1983). The film speed is set at 100 ASA and the meter activated over the radiograph. The recorded exposure time is multiplied by 2000 to give the exposure in seconds for RPC film. Using a cable release and the manual shutter setting on the camera the appropriate exposure for that radiograph is then given. An illuminator with extra fluorescent tubes may be constructed to shorten the exposures (Molter & Alfidi, 1981). Wide apertures also help to do this. The great advantage of this film is that it can be developed in Kodak X-Omat processors in 90 s. Other processors and chemicals are also usually satisfactory. The film may be handled under the usual red safelight and fed through the processor. Cutting and mounting take a few minutes.

2. Agfa Dia Direct is widely used to reproduce radiographs. Its speed is 32 ASA and while many exposures are short enough to hand-hold the camera with a wide aperture, close-ups require a camera stand or tripod. Exposures longer than 1/30th of a second should not be hand-held. The film is cheaper than colour slide film and quite satisfactory.

3. Ordinary colour slide film may be used to reproduce radiographs provided a fluorescent to daylight filter is used with a warm fluorescent tube in the illuminator (Mayer, 1982). However, most

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illuminators have a cold blue tube which gives a blue-green tint to the slide. This can be removed with a CC50M magenta colour correction filter (Dunne & Crandall, 1982). Where exposure times are short, the camera may be hand-held, which saves time and balances the extra expense of the film.

4. Black-and-white print film may be used but requires a reversal processing technique to convert it into monochrome slide film. Kodak and Tetenal both make such processing kits. This method produces very high quality slides, but is troublesome, requires some expertise in development and is not particularly cheap.

5. Polaroid "Instant" slide film is a recent development which is convenient and rapid. Colour slide, monochrome slide and a high-contrast "lith"-type film are available, the latter for text and line drawings. The film is run through an "Autoprocessor" which requires an initial outlay of about £100. Slides may be prepared in 5 min and are of reasonable quality. The films are expensive, however, and for this reason have not replaced Kodak RPC film for routine use in our department.

6. Some multiformat cameras used in ultrasound, nuclear medicine and computed tomography departments can produce 35 mm-size images. These can be cut and mounted directly into slide-holders. They project effectively but may require computer time to retrieve the images for duplication. Some radiographs, such as small joints, can be copied, cut to size and mounted directly in slide-holders (Healey, 1982)

Masking the radiographs is advisable to remove untidy white borders from the slide. We use two L-shaped pieces of black cardboard, which allow rapid adjustment to the size required. If the room is dark, the masking surfaces appear completely black in the slides. Most camera meters are centre-weighed, except for a few very expensive models. This means that a false reading may be obtained, for example, over the mediastinum when the lungs are of interest. Temporarily moving the radiograph to bring the area of interest under the meter or using a hand-held meter instead of the camera meter gives excellent results What is seen through the camera's viewfinder is about 93% of the final image. This means that care must be taken with the borders of some pictures as a larger image than that seen will be produced.

NOTE ADDED IN PROOF

Most departments will have the basic equipment for copying but an estimate of the costs follows.

A 35 mm camera with manual function and a 50 mm lens will cost from £70 upwards Screw-on close-up lenses cost £20, but a macro or macro-zoom lens would cost £100. A table tripod (£15) could substitute for a copy stand (£50) Small items like the filter, filter holder and cable release would not exceed £10 combined

Kodak RPC film in a 150-foot bulk roll costs £30. The cost per 36-frame film is 75 pence and unit cost per mounted slide 4 pence. Kodak Vericolor 5072 costs £40 for 30 m, which produces 25 36-frame films. Commercial development of a film averages £1.50, and unit cost per mounted slide is 10 pence

Agfa-Gevaert have ceased production of Dia Direct.

ACKNOWLEDGMENTS

We thank Dr J. Masterson for helpful advice and Miss J. Rutherford for valuable secretarial assistance.

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Radiological safety: gamma camera flood sources

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Tests of gamma camera field uniformity are often carried out using radioactive "flood" sources. The most commonly used type consists of a plastic disc, incorporating a uniformly deposited thin film of cobalt 57. This is usually sealed in a thin aluminium casing without any additional shielding for gamma rays. Recently, the Nuclear Medicine Committee of the British Institute of Radiology drew attention to

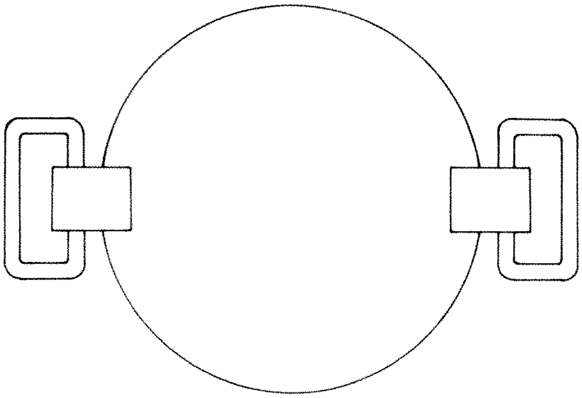

FIG. 1.
Top view of flood source showing construction of handles (not to scale).

radiological safety arrangements which must be made when such flood sources are used.

The Ionising Radiations Regulation 6(5)(a) requires that no radioactive substance in the form of a sealed source is held by hand, or manipulated directly by hand, unless the instantaneous dose rate does not exceed 75 μSv h^{-1}. Dose rates on the surface of a typical source of 185 MBq with active diameters between 330 mm and 600 mm vary between 850 μSv h^{-1} and 120 μSv h^{-1}. Clearly, there is an associated whole-body dose to the operator. An additional hazard arises because the source construction provides an inactive rim of only approximately 1 cm, making it almost impossible to handle without high finger doses being received.

The whole-body radiation dose to the operator may be reduced significantly by the use of lead shielding. It is found that a 1.5 mm layer of lead, glued onto the rear face and around the edge of the source, will reduce the rear surface dose rate for a 470 mm-active-diameter source from 250 μSv h^{-1} to 4 μSv h^{-1}. There is, of course, an increase in weight from 3.4 kg to 6.8 kg. The addition of handles, which can be clamped to the edges of the source make it easy to handle in spite of the increased weight and avoids the need for the fingers to come into contact with the active surface. The construction adopted by us for many departments in the North Western Region is shown in Figs 1 and 2. It should be noted that the source still fits into the manufacturer's supplied carrying box or other protected container.

The addition of lead around the source gives rise to additional scattered radiation accompanying the spectrum of the cobalt 57. However, for cameras with energy resolution of 13% or better and with an energy window of 20% or less, no change can be seen in the pattern of response of the camera. This has been verified by uniformity measurements carried out with and without the lead backing.

The associated written systems of work must detail the manner in which the source is to be used and by whom. They will include: the identification of any "controlled area" existing during the use of the source and specification of the consequential working procedures; the need not to point the front surface of the source towards any person; and the arrangement for regular inspection and testing together with its storage in a closed (and locked?) protective container when not in use.

The addition of the lead to the source, as described, can considerably simplify the implementation of the Ionising Radiations Regulations in this aspect of departmental work.

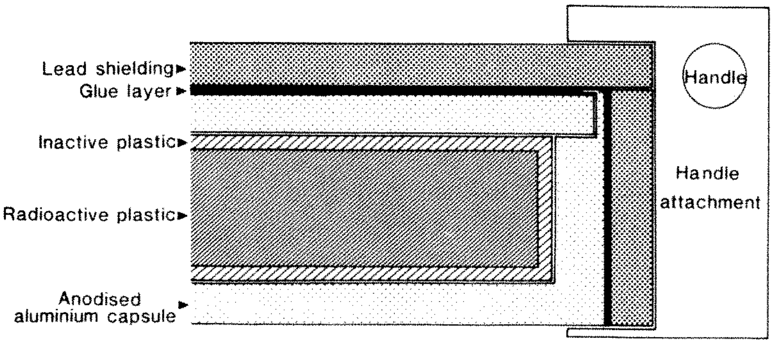

FIG. 2.
Schematic diagram of flood source construction with lead shielding and handle (not to scale).

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Case reports

A photopenic lesion in osteosarcoma

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Primary and secondary bone tumours usually result in areas of increased tracer uptake on bone scans because of osteoblastic reaction of the bone surrounding the tumour (Kirchner, 1980). Rarely, tumours may result in areas of reduced tracer uptake (Georgen et al, 1974; Sy et al, 1975; Goris et al, 1980; Kado et al, 1980; Bushnell et al, 1983; Makhija, 1983; Weingrad et al, 1984). In this report, a case of osteosarcoma with prominent fibroblastic reaction is presented as it resulted in the unusual finding of a "cold" lesion on bone scintigraphy.

CASE REPORT

The patient was a 14-year-old white girl who presented with a 4-month history of a limp and a 3-week history of right hip pain. Radiological examination demonstrated a large destructive lesion in the right femoral neck and intertrochanteric region extending medially into the soft tissues (Fig. 1). A technetium bone scan (Fig. 2) was remarkable in that the known lesion in the right femoral neck demonstrated reducer tracer uptake within it, indicating either interruption of bone blood supply or complete bone destruction by the tumour. Routine investigations revealed no evidence of distant metastatic spread.

An open biopsy of the right femoral neck showed osteogenic sarcoma of fibrosarcomatous (fibroblastic) type and of intermediate grade of malignancy (Fig. 3).

DISCUSSION

Primary malignant bone tumours very rarely cause photon-deficient lesions on $^{99}Tc^{m}$ bone scans (Kado et al, 1980; Weingrad et al, 1984) and only one case of primary fibrosarcoma of bone so doing is reported in the literature (Makhija, 1983). Possible mechanisms to explain this include decreased blood supply due to involvement of cortical nutrient vessels by the tumour and "less bone" due to gross bone destruction and lack of reactive bone tissue (Weingrad et al, 1984). These cases illustrate the fact that bone scans cannot differentiate malignant from benign tumours, as malignant neoplasms, such as the one presented here, can result in photopenic lesions on bone scintigraphy.

Radiologically, this patient presented a considerable diagnostic problem. The radiographs were thought to suggest an aneurysmal bone cyst or giant-cell tumour. The final histology was surprising not only radiologically but because of the rarity of cold lesions on bone scan in this variety of malignancy.

Thorough histological examination of the entire tumour mass revealed large and diffuse areas of necrosis intermingled with regions of viable tumour. The photon deficiency is probably the result of infarcted necrotic areas within the tumour. The blood supply may also be decreased by tumoral obstruction of intralesional blood vessels.

Gallium-67 studies are known to be sensitive in detecting primary bone tumours, such as osteogenic sarcoma and fibrosarcoma (Kaufman et al, 1977; Simon & Kirchner, 1980). They can also help to assess the extent of the tumour and this is particularly useful in cases such as this one, in which there is no reaction on

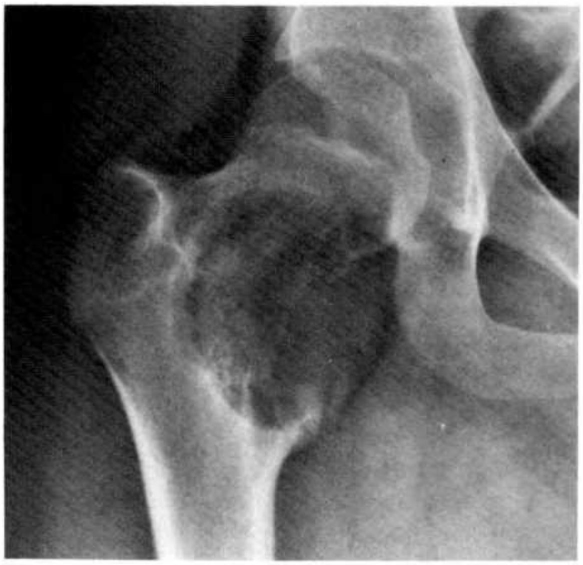

FIG. 1.

Antero-posterior radiograph of the pelvis with a large lytic area in the neck of the right femur.

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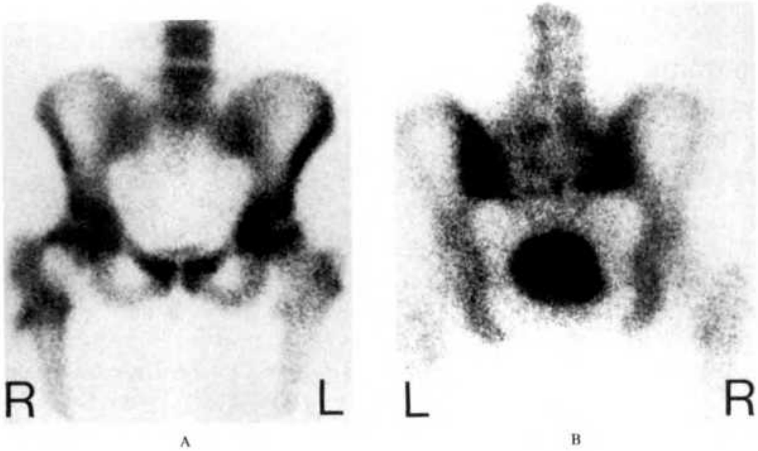

FIG. 2.

Bone scan: (A) anterior and (B) posterior views. A large photopenic lesion can be seen in the upper femur.

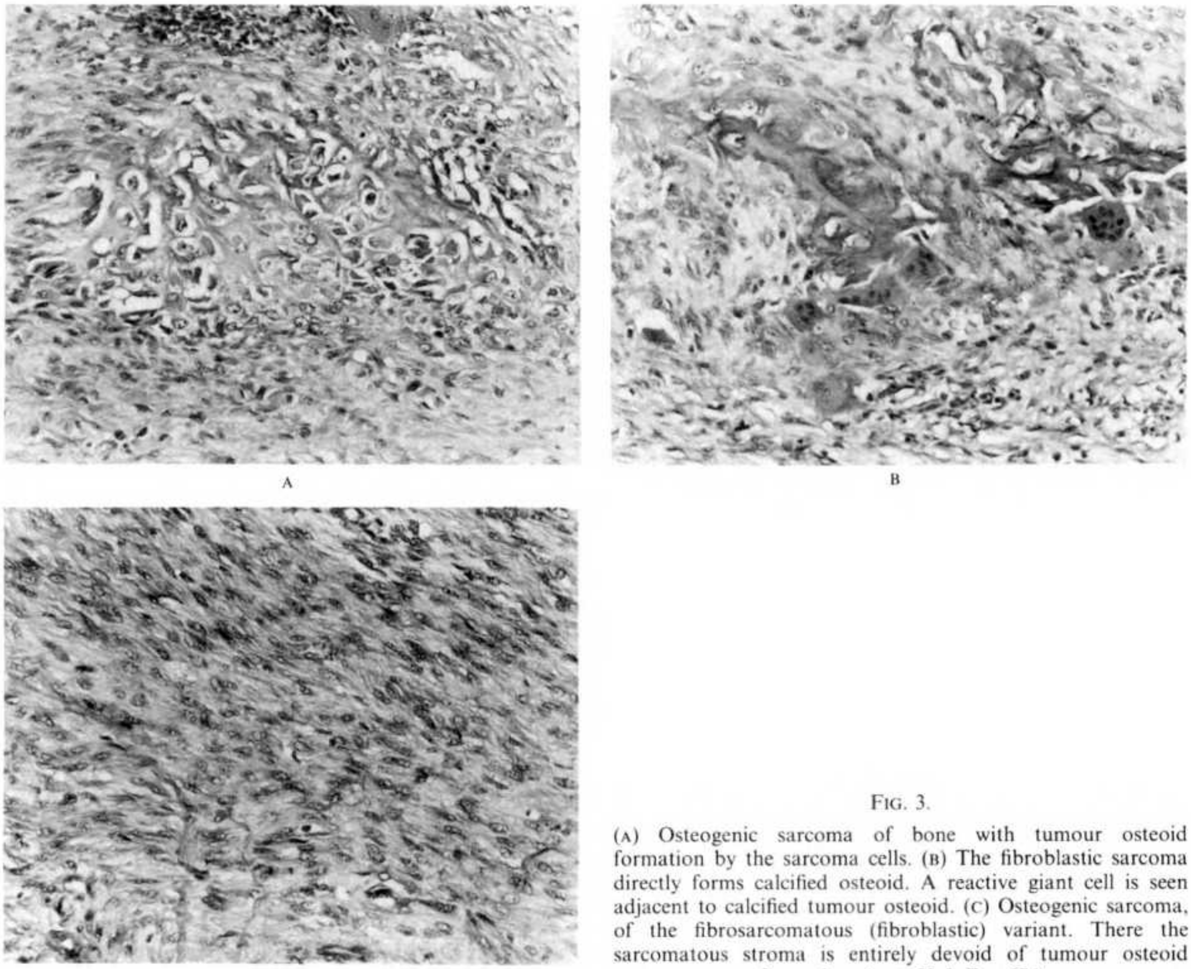

FIG. 3.

(A) Osteogenic sarcoma of bone with tumour osteoid formation by the sarcoma cells. (B) The fibroblastic sarcoma directly forms calcified osteoid. A reactive giant cell is seen adjacent to calcified tumour osteoid. (C) Osteogenic sarcoma, of the fibrosarcomatous (fibroblastic) variant. There the sarcomatous stroma is entirely devoid of tumour osteoid formation. (A–C, H & E ×67.)

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technetium scan. Unfortunately, a gallium scan was not performed

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Magnetic resonance imaging of the dissected thoracic aorta

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Magnetic resonance imaging (MRI) is ideally suited to the examination of the thoracic aorta because of the ability of the technique to demonstrate mediastinal vessels, depict blood flow, and produce direct oblique and sagittal as well as coronal and transaxial images. The authors present a case in which the findings on MRI are compared with angiography and computed tomography (CT) in a patient with an aortic dissection and a thrombus within the false lumen.

CASE REPORT

A 58-year-old man was presented with acute severe precordial and abdominal pain. On admission his blood pressure was 190/130 mmHg An ultrasound examination revealed a dissection of the abdominal aorta Further evaluation included CT and aortography.

The CT examination (Siemens Somatom 3) consisted of precontrast scans of the whole thoracic aorta (contiguous 8 mm scans) At at least three pre-selected levels (aortic root, mid-ascending aorta and aortic arch) a bolus of 40 ml Urografin 76% (Schering AG) was injected and a series of six 6 s scans was taken at each level (slice thickness 8 mm, 1 s interscan delay) (Fig. 1). These three-level dynamic sequences were followed by incremental 8 mm scans from the level of the aortic root to the lower extent of the dissection. Aortography was performed in the left anterior oblique position and the subtraction technique was used (Fig. 2) With these two techniques the diagnosis of a Type-B dissection could be made

The day after admission the pain disappeared. There were no signs of vascular insufficiency and renal function was normal Because of his stable condition and the high operative risk, the patient was treated conservatively with anti-hypertensive drugs

Four months after discharge from hospital, MRI was performed using a 0.5 T system (Philips MSD, Best, Holland). An ungated transaxial spin-echo image (TE 30, TR 250) of the aortic arch was first produced in order to define the angulation for the oblique images. This was followed by five contiguous oblique slices with a slice thickness of 10 mm through the aorta using a multiple slice spin-echo technique (TE 30, TR 700) and cardiac gating. The MR radiofrequency pulse sequence was triggered by the R wave followed by a time delay of 10 ms. As a result, all slices were obtained during the systolic phase and the ascending aorta, the aortic arch with the arch vessels and the descending aorta were clearly defined (Fig 3A)

The origin of the intimal flap (distal to the left subclavian artery) was clearly demonstrated and the flap followed into the abdominal aorta on another slice (Fig. 3B). In the distal part of the aorta an increased signal intensity was noted, indicating the presence of either thrombus or slow-flowing blood within the false lumen of the dissected aorta The diagnosis of a Type-B dissection was thus established and,

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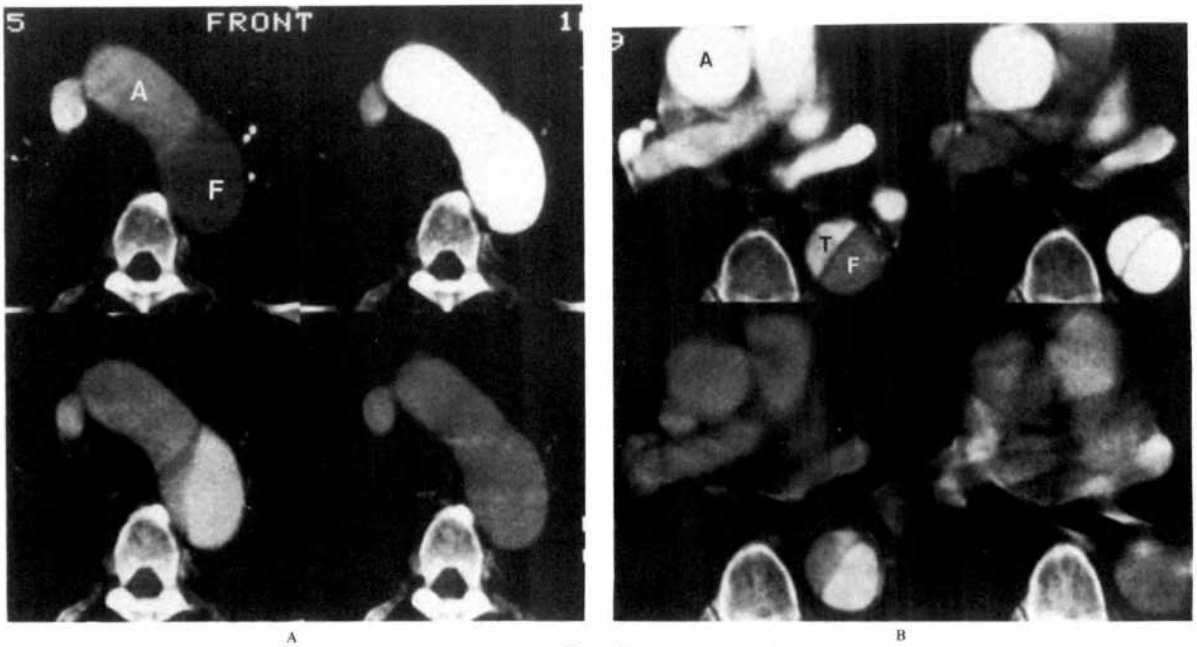


FIG. 1.

(A) A dynamic CT scan at the level of the aortic arch shows sequential filling of the ascending part of the arch (A) and false (F) lumen. Scan interval 6 s. (B) A dynamic CT scan at a lower level shows sequential filling of two lumina; note the intimal flap in the descending aorta. The ascending aorta is normal (= Type B). T = true lumen.

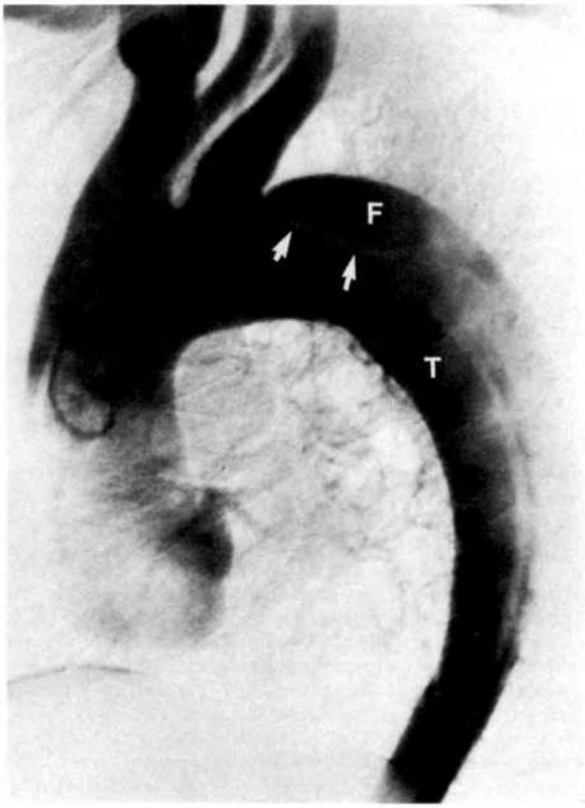
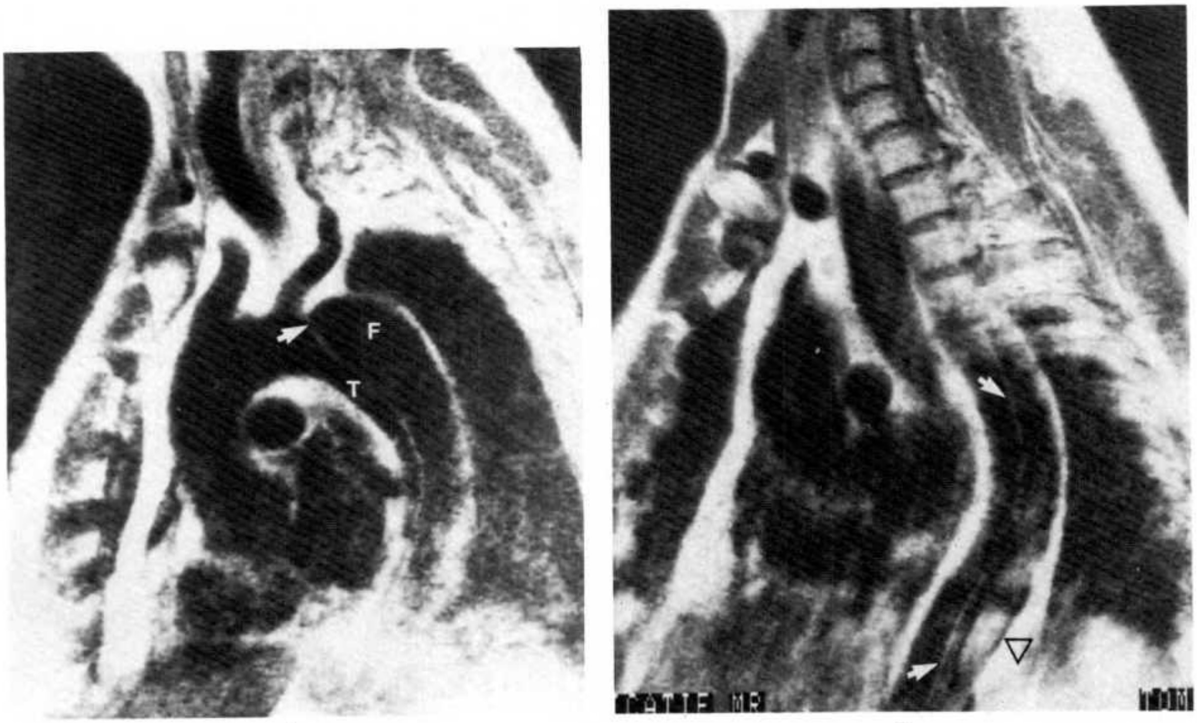


FIG. 2.

A thoracic aortogram (subtraction) in the left anterior oblique projection. A Type-B dissection and intimal flap are seen proximally (arrows). True (T) and false (F) lumina are opacified proximally. In the distal part of the descending aorta, the false lumen and intimal flap are not visualised.



A B

FIG. 3.

Oblique MRI (ECG-gated, TE 30, TR 700) through the ascending aorta, aortic arch and descending aorta accurately depicts the intimal flap separating the true (T) and false (F) lumina in the descending aorta; the intimal flap originates distal to the left subclavian artery (arrow). (B) An oblique MRI (ECG-gated, TE 30, TR 700) slice through the descending aorta. The intimal flap can be followed throughout the course of the descending aorta, even into the abdominal aorta (arrows). Slow flow in the false lumen or thrombus is indicated by intense signal (arrowhead).

because of increased false-lumen size and absence of thrombus formation in the proximal part of the false lumen, a surgical correction of the dissection was performed. The peroperative results confirmed the MRI findings and established that it was, in fact, thrombus in the distal part of the false lumen (Fig. 4).

DISCUSSION

Aortography is the method of choice in diagnosing aortic dissection. Over the past 5 years, however, several publications have recommended the use of CT, and have shown its accuracy to be comparable with or

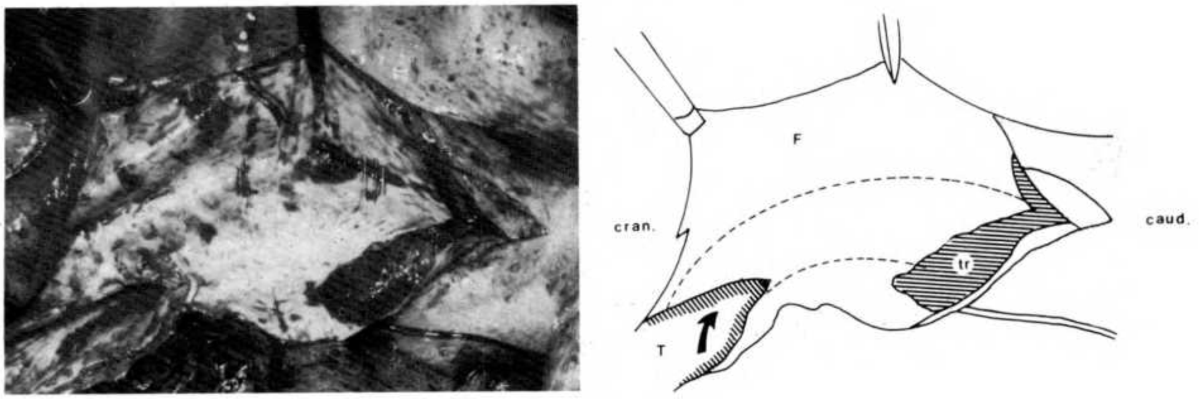


Fig. 4.

Peroperative view. The false lumen (F) is opened. Thrombus (tr) is clearly visible caudally in the false lumen. The true lumen (T) is partly open cranially.

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even better than that of aortography (Oudkerk et al, 1983). Recent reports have shown the potential of MRI in vascular imaging, especially for the thoracic aorta (Amparo et al, 1985). Because of the absence of significant MR signal from rapidly flowing blood, mediastinal vascular anatomy is demonstrated clearly by spin-echo imaging techniques and mediastinal vascular abnormalities are often diagnosed easily without invasive studies.

As is demonstrated in this case, the appearance of a direct oblique image is similar to that of an aortogram but the intimal flap and the false lumen are visualised better with MRI In addition, MRI allows to some extent the evaluation of blood flow or the presence of a thrombus. Both thrombus and slow-flowing blood result in a significantly increased signal from the vessel lumen. The absence of a signal indicates rapid flow in the proximal part of the false lumen (Fig 3B).

A major advantage over both aortography and CT is the ability of MRI to produce direct oblique images as well as avoiding the use of iodinated contrast media.

A subsequent MRI study on another patient with a Type-B dissection showed identical results. These results, supported by those of Amparo et al (1985), suggest that, in future, MRI should become an important imaging modality in the elucidation of aortic dissection

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Ultrasound diagnosis of profunda femoris pseudo-aneurysm following nail-plate fixation of a transcervical femoral fracture

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False aneurysms of the profunda femoris artery as a complication of orthopaedic operative procedures have been well documented in the past They have occurred after osteotomy of the proximal femur (Basset & Houck, 1964; Meyer & Slager, 1964; Dumanian & Kelikian, 1969; Mackenzie et al, 1983), intramedullary nailing of the femoral shaft (Dickson, 1968) and nail and plate operations for neck of femur fractures (Dameron, 1964; Fordyce, 1968; Wolfgang et al, 1974). Although usually pulsatile, several examples of non-pulsatile aneurysms have been reported (Mikulin & Walker, 1984, Read, 1984). Ultrasound is routinely used in the diagnosis of aortic aneurysms and, more recently, in the management of peripheral aneurysms (Davis et al, 1977; Gooding & Effeney, 1980). In the case we describe, ultrasound revealed a false aneurysm of the profunda femoris demonstrating its size and site, where clinical examination was inconclusive.

CASE REPORT

An 85-year-old woman fell at home, sustaining a Garden Stage II transcervical fracture of the neck of the right femur.

She underwent operative reduction and fixation with a four-hole dynamic hip screw introduced over a guide wire through a lateral approach Twelve days after the operation she complained of slight tenderness in her right leg and was noted to have mild, non-tender swelling from ankle to thigh A presumptive diagnosis of deep venous thrombosis was made and she was treated with anti-embolism stockings and mobilisation Her condition improved with mobilisation and she was discharged

Six weeks later she was seen at home and found to have a hard, non-pulsatile, tender mass in the right upper thigh. There were no signs of venous obstruction or arterial insufficiency and no bruit was evident Plain radiography showed a large soft-tissue mass medial to the upper femur The third screw of the nail–plate device had penetrated the medial cortex and the tip lay adjacent to the mass

The history of previous orthopaedic surgery suggested a possible vascular complication and, therefore, an ultrasound examination was performed, using a Diasonics DRF 400 ultrasound machine With both the high-resolution 7.5 MHz and routine 3.5 MHz transducers, good detail of both superficial and deeper tissues was obtained. A solid lesion measuring 12 cm in diameter and less echogenic than the surrounding tissues was demonstrated on the medial aspect of the thigh Within the lower end of the mass was a 3 cm, rounded sonolucent area, which was pulsatile The superficial femoral artery was seen anterior to and separate from the mass. A diagnosis of aneurysm of the profunda femoris artery was made (Fig. 1)

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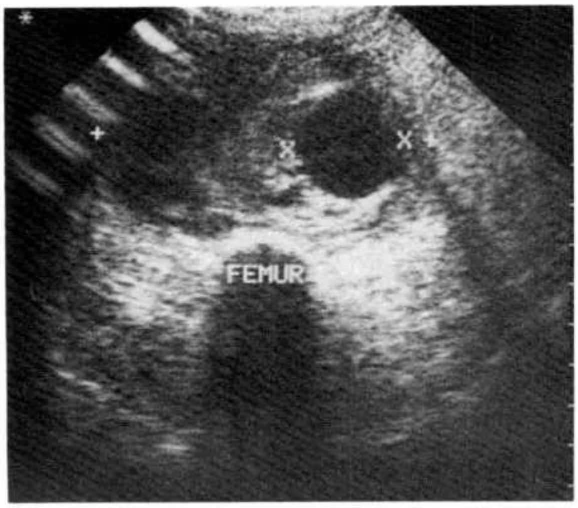

FIG. 1.

Transverse ultrasound scan of medial right thigh showing a large mass of reduced echogenicity with a sonolucent cavity posteriorly. The cavity was seen to pulsate during real-time examination.

Pre-operative arteriography confirmed the presence of a narrow-necked aneurysm arising from the mid profunda femoris artery approximately 10 cm from its origin at the level of the third screw, displacing the vessel medially. The superficial femoral artery (displaced anteriorly) showed mild atheromatous disease (Fig. 2).

At operation the profunda femoris artery was traced down into the thigh for a short distance beyond both the circumflex and the two perforating branches. At this point, marked inflammatory reaction close to the pseudo-aneurysm was encountered. Definitive ligation of the profunda femoris artery was performed above the aneurysm. The post-operative recovery was unremarkable and after 5 days there appeared to be a reduction in the size of the mass.

Follow-up ultrasound 1 week after operation showed the aneurysm cavity now full of clot (Fig. 3).

DISCUSSION

The initial post-operative presentation of deep venous thrombosis may have resulted spontaneously or from aneurysm-induced femoral vein compression. The latter has been shown previously (Pappas et al, 1964; Campbell et al, 1983) and should be considered in patients who have recently undergone hip surgery

Our patient had no previous history to suggest vascular disease. In view of the early presentation after operation, and the evidence of screw penetration of the femoral cortex adjacent to the aneurysm, it seems clear that the aneurysm was a direct result of the orthopaedic procedure.

Most profunda femoris aneurysms are thought to be due to penetration by a drill bit or screw at operation, but Wolfgang et al (1974) presented a case occurring 14 years after operation and postulated that gradual erosion of the vascular wall by hip motion or trauma

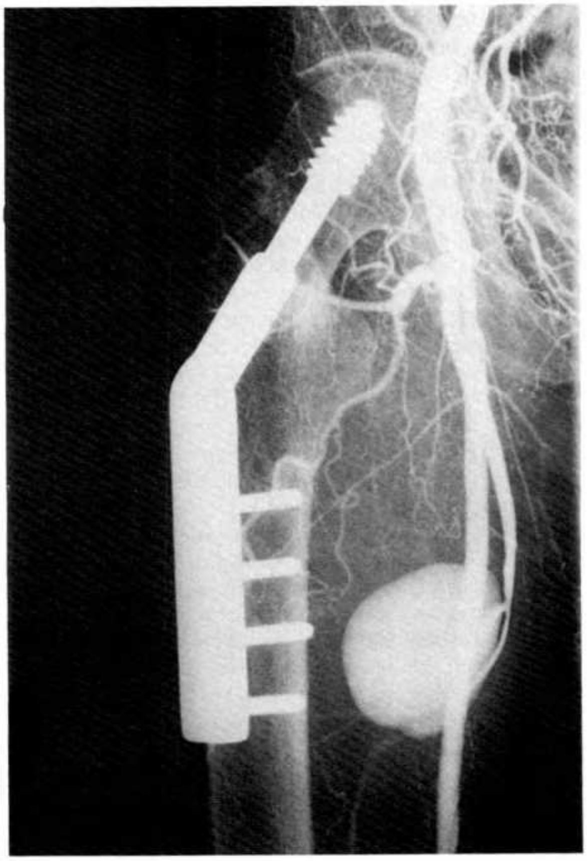

FIG. 2.

Arteriogram confirming a false aneurysm of the distal profunda femoris artery displacing the vessel medially. The third screw of the nail–plate device has penetrated the cortex.

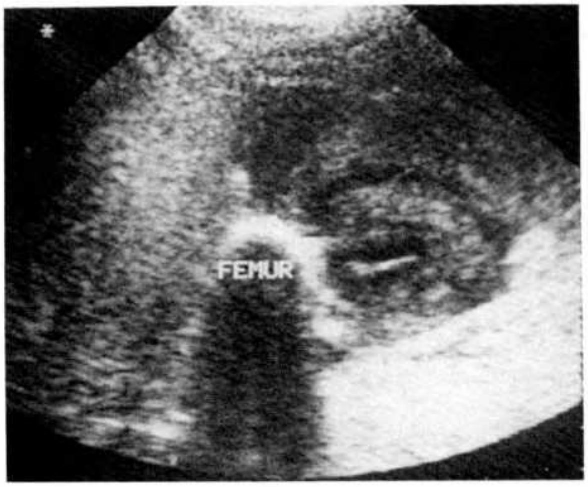

FIG. 3.

Follow-up transverse ultrasound scan of anterior right thigh shows the cavity now full of clot (1 week after operation). No pulsation was seen.

must be another cause. A further predisposing factor is thought to be malplacement of bone levers which may fix the profunda femoris branches to the medial femoral cortex, thus encouraging penetration by the drill (Fordyce, 1968). Of the nail–plate operations reviewed, most aneurysms occurred at the third or fourth screw level where the adjacent medial femoral cortex had been penetrated by a screw (Wolfgang et al, 1974).

A false aneurysm is originally an encapsulated haematoma arising from a leaking artery. Unlike a true aneurysm, it does not have a true wall, and is therefore more likely to expand, being confined only by surrounding soft tissues. As it develops, a smooth lining will form and organisation of clot occurs.

Classically, false aneurysms present with a tender pulsatile mass with or without signs of ischaemia, venous obstruction or haemorrhage (Ochsner, 1982), but several reports have shown that not all aneurysms are pulsatile (Mikulin & Walker, 1984; Read, 1984). Clinically, the pulsatile element and bruit are very important as they suggest a vascular aetiology when a mass is detected. Lack of pulsatility is thought to result from: a large amount of thrombus attached to the wall of the aneurysm, damping pulsation; the defect in the arterial wall being too small to allow a clinically detectable pulsation (Mikulin & Walker, 1984); or the aneurysm being too tense to pulsate (Read, 1984). In this case it was thought to be a result of mural thrombus.

Femoral aneurysms are well demonstrated by ultrasound and high-resolution transducers can give accurate assessment of their size and configuration as well as demonstrating the cavity and thrombus. This is a definite advantage over arteriography, where only the cavity is shown.

In considering treatment, if there is good flow through the superficial femoral artery, the distal branches of the profunda femoris artery can be ligated without distal vascular impairment. Transcatheter embolisation has a role to play (Barnes & Broude, 1985) being safe, rapid, and effective and avoiding operative morbidity. However, this method may have limitations in the elderly patient with significant atherosclerosis in the superficial femoral circulation and surgical treatment may be preferred.

In conclusion, traumatic aneurysms of the profunda femoris artery have been well documented in the past and usually present no difficulty in diagnosis if the classic signs are present. In the case discussed the diagnosis was not clinically obvious at first but later suspicion was confirmed by ultrasound.

Acknowledgments

We would like to thank Dr G R. Sutherland for helpful advice and Mrs J Stewart for typing the manuscript.

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1987, *The British Journal of Radiology*, *60*, 505–506 MAY 1987

Case reports

Massive hypertrophy of the lingual tonsils: an unusual cause of dysphagia

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Small aggregates of lymphoid tissue are a normal finding at the back of the tongue. The lymphoid tonsil has been defined as the lymph tissue between the epiglottis posteriorly, the circumvallate papillae anteriorly and the tonsillar pillars on each side of the tongue (Hoover, 1934). The most common abnormalities of the lingual tonsil are hyperplasia and lingual tonsillitis (Joseph et al, 1984). Hypertrophy of the lingual tonsil usually occurs around puberty and is rarely of any clinical significance. We have recently encountered a patient with a 3-year history of severe dysphagia due to massive hypertrophy of the lingual tonsils, and describe the appearances on fluoroscopy and computed tomography (CT).

CASE REPORT

A 56-year-old man was referred by his general practitioner, complaining of severe dysphagia for liquids and solids which had been worsening progressively for over 3 years. He had a slight cough and had had several episodes of aphonia. There was a past history of tonsillectomy and penicillin allergy.

A lateral neck radiograph revealed a large polypoidal mass above the epiglottis and a barium-swallow examination demonstrated a large villous mass occupying both valleculae and piriform fossae with a narrow open channel in between (Figs 1, 2). The extent of the mass was confirmed using CT, which showed obstruction of the oropharynx but no bone destruction (Fig. 3). At direct laryngoscopy, biopsies were taken which showed benign hyperplastic lymphoid tissue with no evidence of malignant change. The patient's symptoms abated spontaneously and surgery has been postponed.

Requests for reprints to Dr Patricia Fitzgerald.

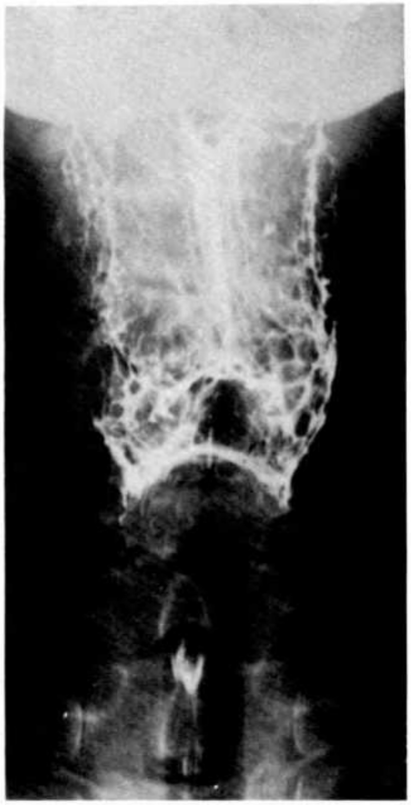

FIG. 1.

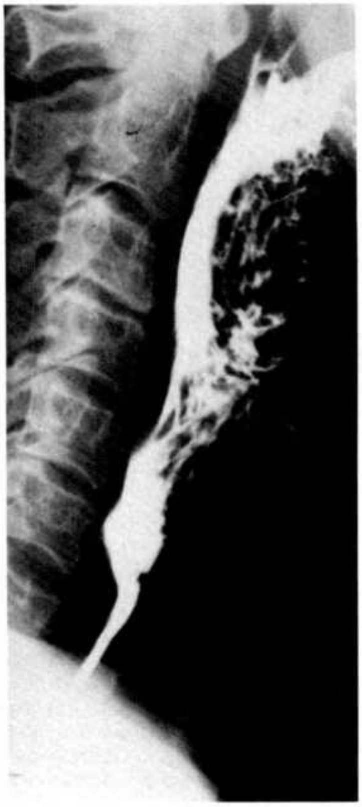

FIG. 2.

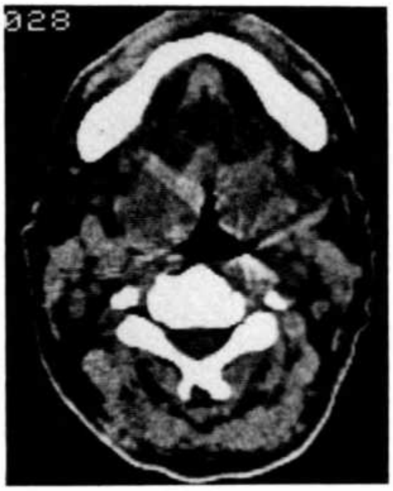

FIG. 3.

A CT scan shows marked narrowing of the oropharynx.

FIG. 1.

Barium-swallow radiograph showing a large mass occupying both valleculae and piriform fossae.

FIG. 2.

Lateral view showing the corrugated appearance of the oropharyngeal mass.

1987, *The British Journal of Radiology*, *60*, 506–508

Discussion

Small aggregates of lymphoid tissue are common at the base of the tongue. Enlargement of the lymphoid tonsil may occur around puberty or may be associated with allergy or infection (Gromet et al, 1982). Massive enlargement of the lingual tonsil, however, is rare and there are few reports of associated dysphagia or respiratory obstruction. Clinical symptoms also include cough and dysphonia. Hypertrophy of the lingual tonsil is a recognised cause of sleep apnoea (Olsen et al, 1981).

Plain radiography of the neck and a barium-swallow examination will delineate the site, size and extent of the mass. In this case, the surface of the mass had a corrugated appearance with barium outlining the interstices of the enlarged lymphoid tissue.

The differential diagnosis of enlarged lingual tonsil includes lymphoma, lingual thyroid and granular cell myoblastoma (Neinas et al, 1973; Weider & Parker, 1977; Gromet et al, 1982; Joseph et al, 1984). The appearances at laryngoscopy are frequently characteristic and some authors believe biopsy to be unnecessary (Gromet et al, 1982). However, when the mass is irregular and nodular it may not be possible to distinguish the benign entity from tumour. The radiologist should be aware of this entity as an unusual cause of bizarre filling defects in the oropharynx.

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Demonstration of a lactobezoar by ultrasound

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Lactobezoar is a relatively uncommon disorder first described by Wolf and Bruce (1959). The diagnosis has usually been confirmed radiologically or by gastroscopy.

We present a case of a lactobezoar diagnosed by ultrasound To our knowledge, this is the first description of the ultrasonic appearances of this condition.

Case Report

A previously healthy 4-month-old boy was admitted to hospital with symptoms of crying and vomiting. He weighed 6.2 kg on admission and was being fed on a modified formula feed and solids.

On examination, there was a slight pyrexia of 37.8°C and neck stiffness. A lumbar puncture, blood cultures and mid-stream urine specimens helped to exclude meningitis and infections at other sites A chest radiograph was normal and an abdominal radiograph was reported as showing a prominent stomach outline. The patient had not had a recent feed to account for this. On this occasion, the child appeared to improve without treatment and was discharged

He was readmitted 10 days later, with symptoms similar to those of the first admission but a firm mass was now clearly palpable in the left hypochondrium, extending into the epigastrium. A plain abdominal radiograph again showed a distended stomach and the erect radiograph demonstrated a mass with a convex upper border (Fig. 1).

In view of the palpable mass, an ultrasound examination was performed to exclude the possibilities of an enlarged spleen or a mass related to the left kidney; this demonstrated a normal spleen and a normal left kidney and suprarenal region The stomach appeared distended and contained a "mass" This showed a definite margin with a hyperechoic and mixed-echo texture. A clear-water feed helped to outline the mass, which followed the outline of the stomach (Fig 2) The child had not been fed for at least 6 h prior to ultrasound and a diagnosis of a lactobezoar was suggested.

There was spontaneous remission of symptoms over the next few days and the mass was less obvious upon clinical examination

A repeat ultrasound examination 10 days after the initial study, once again with a clear-water feed, showed that the mass was nearly half the size it was at the previous examination and also showed evidence of its breaking up. The surface was irregular and there were pieces of debris floating above the upper border (Fig 3)

Gastroscopy was performed a week later and showed that the stomach was now clear. The patient at this stage was very well and the vomiting had completely subsided. Repeat ultrasound examination showed a clear stomach

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Correspondence to Dr D. R. Naik

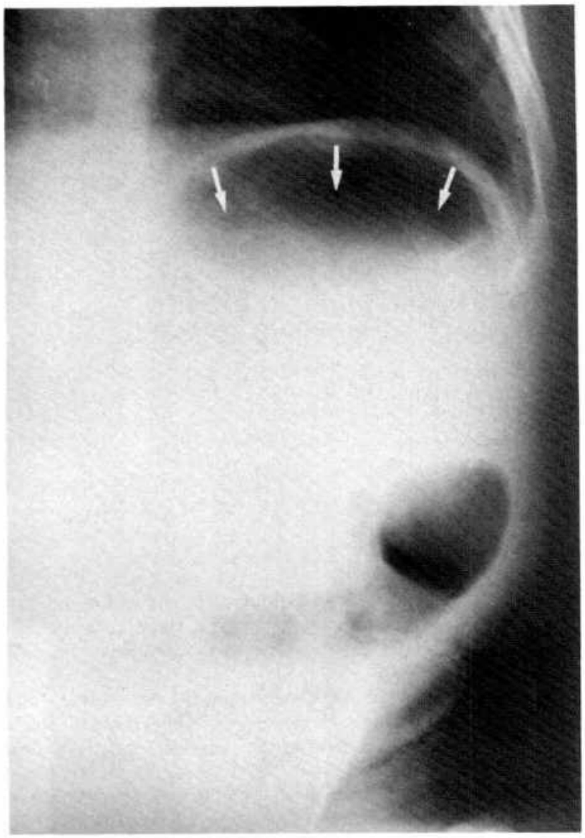

FIG. 1.

An erect radiograph of the upper abdomen taken prior to ultrasound examination shows a "mass" with convex upper border (arrows) within the gastric air bubble. Note: there is *no* fluid level.

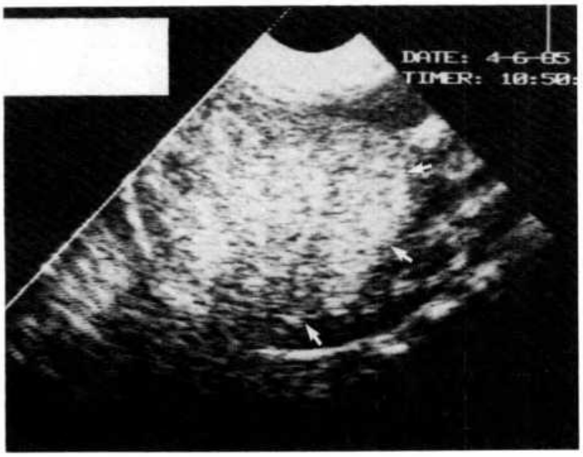

FIG. 2.

An oblique scan from the epigastrium along the long axis of the fundus and body of the stomach shows the hyperechoic "mass" within a non-uniform mixed-echo texture of the lactobezoar (arrows), outlined by clear-water feed.

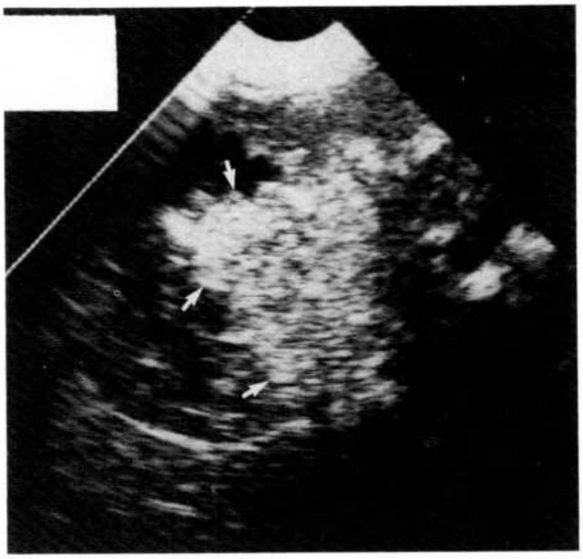

FIG. 3.

The mass is seen broken up: the outline is now irregular (arrows), and loose debris is seen floating in the water feed.

DISCUSSION

The formation of lactobezoar has been attributed to powdered milk when mixed with an inadequate amount of water, which forms a coagulum in the stomach of an infant (Wolf & Davies, 1963). Normal feeding schedules may also result in the formation of a lactobezoar as seen in two cases reported by Cremin et al (1974). This may be due to another postulated cause in premature infants, *i.e.* insufficient enzyme capability to digest the formula preparation (McCollough, 1962; Sullivan & Smith, 1977). The incidence of lactobezoar in pre-term infants may be increasing because of the increasing use of pre-term formula feeds (Schreiner et al, 1979).

As in this case, the lactobezoar may be palpable and hence mistaken for a tumour clinically.

Abdominal radiography and barium examinations suggest the diagnosis, and confirmation is achieved by gastroscopy and surgery. In this case, the clinical findings and the ultrasound appearances were highly suggestive of a lactobezoar.

Treatment involves conservative management with intravenous rehydration and temporary stopping of feeding, followed by a change of feed and/or a proper schedule of correctly mixed feed if this is thought to be the cause of the lactobezoar. Spontaneous remissions can also occur, as seen in this patient.

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The radiological findings in torsion of an appendix epiploica

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(*Received May 1986 and in revised form July 1986*)

The appendices epiploicae are fat-laden pouches of visceral peritoneum on the wall of the large bowel. Rarely they may be found on the vermiform appendix.

Torsion or inflammation of the appendices epiploicae, although known to surgeons as a mimic of appendicitis or diverticulitis, is rarely diagnosed pre-operatively. To our knowledge, this is the first report of the radiological appearances of this condition.

CASE REPORT

A 30-year-old man presented with pain in the left iliac fossa (LIF), which had suddenly begun 24 h previously. It was continuous in character and not associated with any alteration in bowel habit, bleeding per rectum or melaena. On examination, the only finding was a small (5–6 cm) mobile mass in the LIF with localised tenderness, guarding and rebound. Laboratory investigations were all within normal limits (erythrocyte sedimentation rate = 1 mm/h, white cell count = 6.6×10^9/l). The working diagnosis was paracolic abscess.

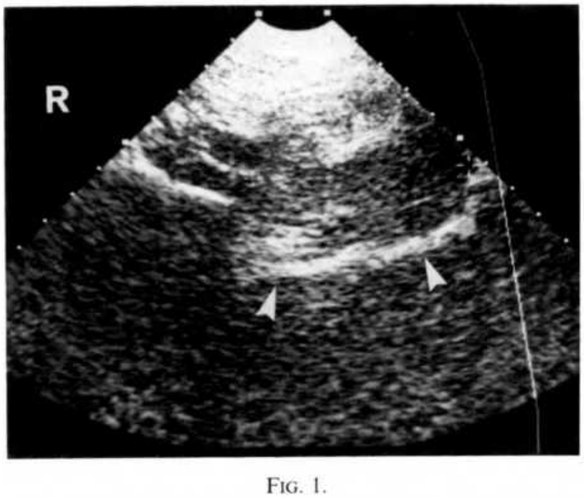

FIG. 1.
A transverse ultrasound scan showing LIF mass (arrowheads) measuring 5 cm by 6 cm.

A plain radiograph of the abdomen was normal and ultrasound of the LIF demonstrated a multilobular, finely echogenic, 5 cm × 6 cm mass at the point of focal tenderness (Fig. 1) which was reported as a possible nodal mass. Sigmoidoscopy 2 days later showed no intrinsic abnormality of the colon. A water-soluble barium enema (in order not to delay computed tomography) confirmed the absence of colonic disease but showed extrinsic compression of the lateral wall of the sigmoid colon, corresponding to the palpable mass (Fig. 2). An ultrasound-guided biopsy was then attempted but this proved difficult owing to the mobility of the mass and the tissue obtained was not diagnostic, consisting of tiny fragments of acellular debris, some adipose tissue and a fragment of colonic mucosa. Computed tomography 10 days after presentation failed to show any abnormality (Fig. 3). The mass was now judged on clinical examination to have halved its size, but as the patient was still complaining of considerable pain, a diagnostic laparotomy was performed.

At surgery a firm, 2–3 cm nodule adherent to the sigmoid colon was excised and showed a cystic structure filled with brown material. Histology showed it to consist of fatty tissue with focal ischaemic changes, the appearance of torsion of an appendix epiploica.

DISCUSSION

The appendices epiploicae are arranged in two rows along the bowel wall. They have no known natural function but may be useful to surgeons in helping to protect a suture line or close a perforation (Sabiston, 1977). They may be involved in a number of disease processes, the commonest being epiploic appendicitis, which may be secondary to torsion or thrombosis. This affects mainly those appendices in the caecal and sigmoid regions and is a differential diagnosis in appendicitis and diverticulitis (Schwartz, 1984). The symptoms may be minimal or patients may complain of

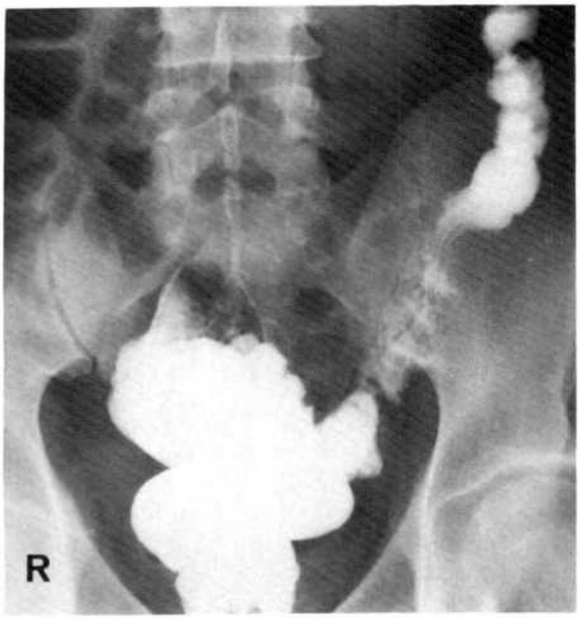

FIG. 2.
Water-soluble barium enema showing extrinsic compression of the lateral wall of the sigmoid colon.

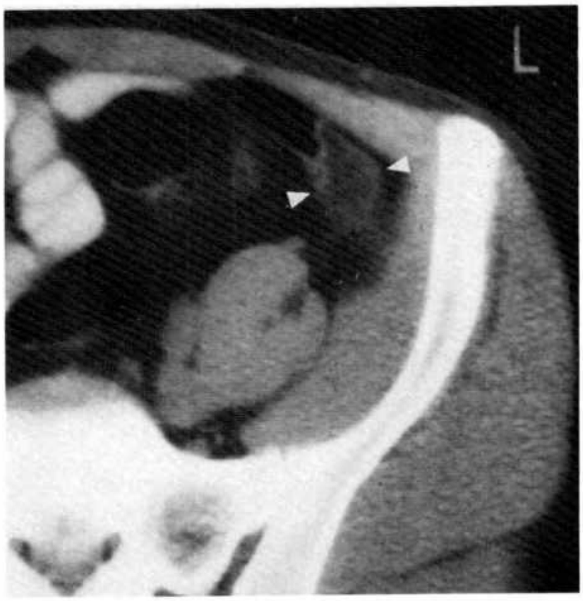

FIG. 3.
Axial computed tomogram over the area of tenderness. Streaky increase in fat density extending to the left iliacus is seen (arrowheads).

continuous right- or left-sided abdominal pain in an area corresponding to the contour of the bowel wall. Usually patients do not look ill; nausea and vomiting are unusual and, unlike appendicitis, appetite is rarely affected. There is localised tenderness, often with marked rebound, but no rigidity. The condition is seldom diagnosed pre-operatively. Treatment is excision with care not to open an associated diverticulum. Other disease processes which may affect the appendices epiploicae include acute and chronic inflammation secondary to diverticulitis, degeneration to form an intraperitoneal loose body, initiation of an intussusception and incarceration within a hernia.

This case proved a radiological diagnostic problem as the authors were not aware of the condition. Clinically, the diagnosis appeared to be diverticulitis but there was no evidence of diverticular disease on the barium enema. A local walled-off perforation due to a foreign body was considered. Computed tomography failed to demonstrate a mass but perhaps, in retrospect, there is a streaky area of increased fat density extending from the lateral aspect of the colon towards the iliacus muscle. The value of careful assessment of abdominal fat on computed tomography has been recently reported (Dixon & Nightingale, 1984; Katz et al, 1985).

Neither torsion nor inflammation of the appendices epiploicae is often diagnosed acutely. They should be considered in the radiological differential diagnosis in patients without evidence of other colonic disease such as Crohn's disease or diverticular disease, either of which may cause an abscess or inflammatory mass. A small extrinsic large-bowel mass with a lobulated, finely echogenic appearance on ultrasound and subtle alterations in the surrounding peritoneal fat density on computed tomography may be the only abnormal findings.

ACKNOWLEDGMENTS

We wish to thank Dr L. Ralph for permission to reproduce the computed tomogram and also Mrs B. Skevington and Mrs Y. Steel for their help in preparing the manuscript.

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List of referees 1986

The following is a list of all those people not on the Editorial Committee who, during 1986, have refereed papers submitted to the *British Journal of Radiology*. With grateful thanks from the Editors and apologies for any errors or omissions.

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MAY 1987

Case of the month

An epidemic tumour

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(*Received July 1986*)

A 40-year-old homosexual man presented with a history of vague, increasing abdominal pain, weight loss and fatigue, but no fever. He gave a past history of multiple episodes of sexually transmitted infection, including hepatitis B and genital herpes. On examination, he was noted to have a faint purple macular and nodular skin rash and generalised lymphadenopathy. Examination was otherwise unremarkable. Routine blood count and chest radiography were normal, and biochemical analysis showed a low serum albumin level (31 g/l) but no other abnormality. The patient had antibodies to HTLV III virus. A barium meal was requested. Figures 1 and 2 show two radiographs from this examination.

What does the barium meal show, and what is the differential diagnosis?

What should be the next investigation?

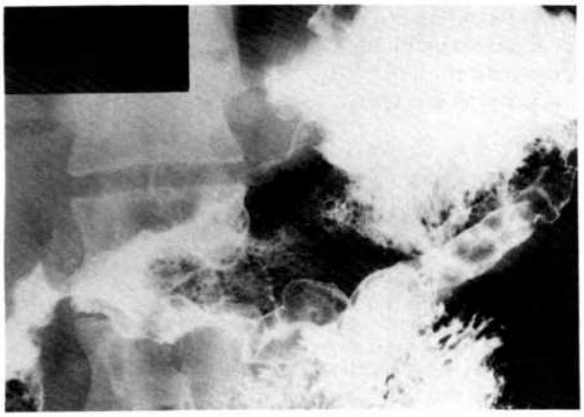

FIG. 1.
Supine radiograph from the barium meal.

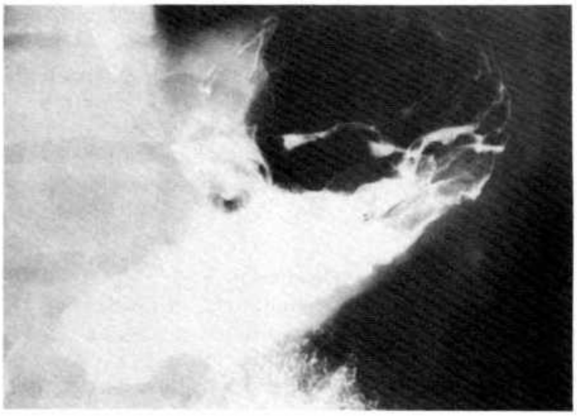

FIG. 2.
Erect radiograph from the barium meal.

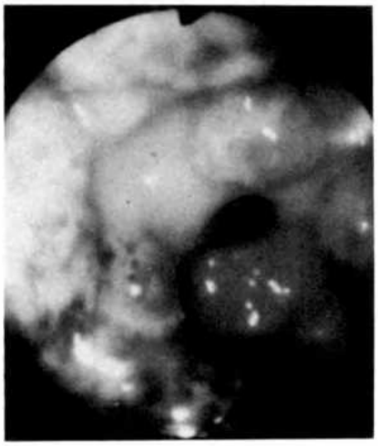

FIG. 3.
Endoscopic photograph of the pyloric region of the stomach. Note the grossly thickened and oedematous folds. Several polypoid lesions are also seen.

The barium meal shows a rigid stomach with grossly thickened and rather nodular folds. The differential diagnosis includes lymphoma, metastases, polyps, carcinoma and Crohn's disease. In a patient with this history, Kaposi's sarcoma should be suspected. An upper gastrointestinal endoscopy was carried out (Fig. 3) and showed the characteristic appearances of Kaposi's sarcoma (KS) involving all the stomach and the first part of the duodenum. This was confirmed by endoscopic biopsy. There was no evidence of opportunistic infection. The skin rash was that of KS, and the diagnosis is acquired immune deficiency syndrome (AIDS).

DISCUSSION

Kaposi's sarcoma, a multifocal neoplasm of the reticulo-endothelial system, is found in about a third of homosexual AIDS cases in the USA. It is, however, rare in heterosexual AIDS patients, for example those who are haemophiliacs, drug abusers or from Haiti (Rose et al, 1982). Kaposi's sarcoma is one of the criteria which establish a diagnosis of AIDS (Muggia & Lonberg, 1986). The condition was, however, first described by Kaposi in 1872 occurring predominantly in the lower limbs of elderly men of Italian or East European Jewish origin—the so-called classic KS. The AIDS-related or epidemic KS resembles a variant quite common in Uganda, where it accounts for 3–9% of all malignancies.

Kaposi's sarcoma almost invariably involves the skin, with pink or purple macules, papules and nodules (Muggia & Lonberg, 1986). Gastrointestinal involvement is common, being seen in 77% of cases at post-mortem examination in a recent series. An antemortem diagnosis of the bowel involvement was, however, made in only 40%; the upper gastrointestinal tract was involved in 32% and the large bowel in 20% of patients (Friedman et al, 1985).

The radiological features of bowel involvement with KS are nodularity and thickening of the mucosal folds, which is seen in 66% of patients. Polypoid lesions are less common, being seen in 18% (Wall et al, 1984). The lesions are frequently multifocal and associated with opportunistic infection of the gastrointestinal tract, particularly candidiasis (Wall et al, 1986).

The diagnosis is more likely to be made by endoscopy than radiology and, indeed, the appearance at endoscopy may be so characteristic that biopsy is unnecessary. Complications described include haemorrhage, obstruction, perforation and malabsorption. These are all unusual and visceral KS rarely produces symptoms. It is, however, associated with a poor prognosis compared with skin KS alone, although the deaths are not directly due to KS but to the associated opportunistic infections (Friedman et al, 1985).

As the AIDS epidemic continues, and as KS is such a common manifestation of the disease, gastrointestinal involvement is likely to be an increasingly common radiological diagnosis.

ACKNOWLEDGMENTS

Our thanks are due to Dr B. Gazzard for permission to report this case and to Dr J. A. Gleeson for helpful advice.

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1987, *The British Journal of Radiology*, 60, 513–515 MAY 1987

Short communications

Analysis of wasted X-ray films: experience in two Kuwait hospitals

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Analysis of the frequency with which radiographs are repeated gives a measure of the quality of work done in a radiology department It provides baseline data for quality-control procedures and offers the possibility of reducing exposure of patients to radiation, and of making economies in the use of films, chemicals and time (McKinlay & McCauley, 1977).

We have analysed the wastage in two hospitals in Kuwait, and report the results

METHOD

Two 700-bed hospitals were examined over a 6-month period, from November to April 1983–84 Each hospital carried out about 125 000 radiographic examinations annually Rejected films were collected from general X-ray rooms and marked with the date and room from which they came. The angiography, mammography and computed tomography (CT) rooms were not included in the survey. The total number of films used daily was recorded by the darkroom technicians.

The rejected films were analysed each week and the reasons for rejection and the type of examination recorded. The reasons were grouped into nine main categories These were:

- Over- and under-exposure.
- Positioning faults.
- Artefacts, including jewellery on patients
- Motion artefacts.
- Equipment faults, including exposure, grid and collimation errors
- Processing faults, including roller marks and films stuck together.
- Film handling, including static, scratches and badly loaded films
- Fogging.
- Check films, used to assess processors or machines.

A "retake" was defined as any radiograph that had to be repeated, so exposing the patient to further radiation, because of some error, breakdown or failure of the radiographic process. The "retake rate" was defined as the proportion of rejected films in relation to the total number of films exposed, and the "reject rate" was the number of reasons for rejecting the film in relation to the total number of films exposed.

RESULTS

The study showed that the average retake rates were 9% and 6% and the reject rates were 13% and 9% from Hospitals 1 and 2 respectively. The weekly analysis of retake and reject notes is shown in Fig. 1. The elevation in the reject rate in Weeks 8 and 9 from Hospital 1 was due to equipment malfunction in one of the rooms, and that in the 12th week was due to a change in staff which resulted in film fogging. Poor-quality films taken by trainees accounted for some of the variation, while in Hospital 2 there was a more constant reject and retake rate.

In Hospital 1 positioning and underexposure were the causes of over 50% of the rejected films (Table I), while equipment faults and both over- and underexposed films were the major causes in Hospital 2.

It is apparent that radiographs of the chest and abdomen were most often repeated (Table II), and that in Hospital 1 this

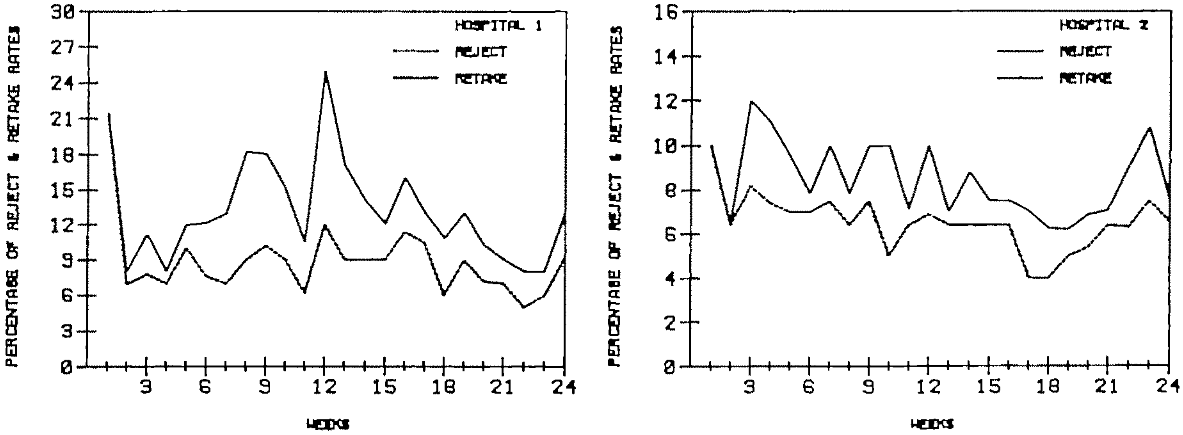

FIG. 1.

Reject and retake rates in both hospitals

TABLE I

THE PERCENTAGE FREQUENCY OF PRINCIPAL CAUSES FOR REJECTS

	Hospital	
	1	2
Positioning error	32	22
Too light	23	21
Too dark	17	16
Fog	17	11
Others	11	18

was usually because of positioning faults, whilst in Hospital 2, there was no one main cause.

The average exposure per retake has been calculated by multiplying the average skin dose in the primary beam (United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), 1977; Kereiakes & Rosenstein, 1980) by the usual area of the X-ray beam used with a normal film size (Goldman & Beech, 1979) to obtain the surface integral of exposure (Table III). We found that the 7.5% retake rate involved 4.2% of patients, who had an average of 1.8 additional radiographs. Using the convenient, conceptually simple but now generally discontinued units R cm^2, the average value of the surface integral of exposure per retake was 551 R cm^2, so that those patients having repeated radiographs received an average of $1.8 \times 551 = 991.8$ R cm^2.

The cost of retakes has also been considered. The two hospitals each used about 250 000 films each year, and around 1.3 million films are used in the government hospitals in Kuwait annually (RPD, 1984). If the cost of every retake is considered to be £5.33, including the cost of film, chemicals, tube life, and the time of radiologists and radiographers, every 1% decrease in the retake rate would save over £66 600 each year (assuming \$1.50 = £1.00).

DISCUSSION

The information generated by this analysis of retakes has helped both hospitals to take corrective action and in some instances to replace equipment, such as faulty cassettes and timers. There is inevitably some anxiety amongst staff when an analysis of this type is carried out, and there has to be reassurance about the objectives of the study before it commences.

It is difficult to decide what an optimum retake rate should be. The average in our two hospitals studied was 7.5%, and it is likely that by continuing the assessment and developing a greater awareness among staff of the causes leading to retakes, the rate might consistently be maintained at about 5%. Retake analysis offers a relatively cheap method of quality assurance which causes little interference in routine work and which helps in reducing both radiation dosage to patients and the cost of examinations.

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TABLE II

PERCENTAGES OF REASONS FOR RETAKE FROM DIFFERENT TYPES OF EXAMINATIONS IN THE TWO HOSPITALS. THE VALUES IN PARENTHESES ARE FROM THE SECOND HOSPITAL

Reason for retake	Examination type				
	Chest	Abdomen	Pelvis	Skull	Extremities
Dark	27 (30)	20 (26)	16 (18)	18 (27)	21 (31)
Light	23 (28)	28 (32)	16 (40)	27 (15)	35 (36)
Positioning	38 (27)	36 (25)	48 (36)	42 (39)	32 (21)
Motion	7 (8)	12 (13)	13 (–)	7 (13)	3 (3)
Others	5 (7)	4 (4)	7 (6)	6 (6)	9 (9)

TABLE III

SURFACE INTEGRAL OF EXPOSURE FOR EACH CATEGORY OF EXAMINATION AND AVERAGE VALUE/RETAKE

Examination type	Percentage of retakes	mR per radiograph	Film size (cm)	Surface integral of exposure (R cm^2)
Chest	26.5	26	35 × 42.5	38.70
Abdomen	31.0	641	35 × 42.5	593.50
Skull	17.0	480	25 × 30.0	360.00
Cervical spine	4.5	259	25 × 30.0	194.30
Thoracic spine	1.5	400	35 × 42.5	595.00
Lumbar spine	7.0	884	35 × 42.5	1314.90
Pelvis	3.5	1343	35 × 42.5	1997.70
Extremities	9.0	100	20 × 25.0	50.00

Average value/retake = 551 R cm^2

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Digital ionography: preliminary results

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In order to ensure the widespread application of information technology to departments of medical imaging, there is a real need to develop a digitally compatible, film-replacement, radiographic imaging system. The feasibility of employing digital ionography in this capacity has been demonstrated (Moores et al, 1984, 1985) using a laboratory prototype system.

We wish to present preliminary results produced by the clinical prototype digital ionography system in order to demonstrate its imaging capability as well as indicate the overall potential of this technology.

MATERIALS

A large-area ionography chamber, which has been outlined previously (Booler et al, 1985), is used to produce latent electrostatic images. These resultant images are read directly by means of scanning electrometers, and the resultant signals are amplified, sampled and stored in a display memory. The digital imaging data are displayed on a high-resolution 1600-line television system, corresponding to a 1600 × 1200 pixel image format with 12 bits of grey-scale per pixel.

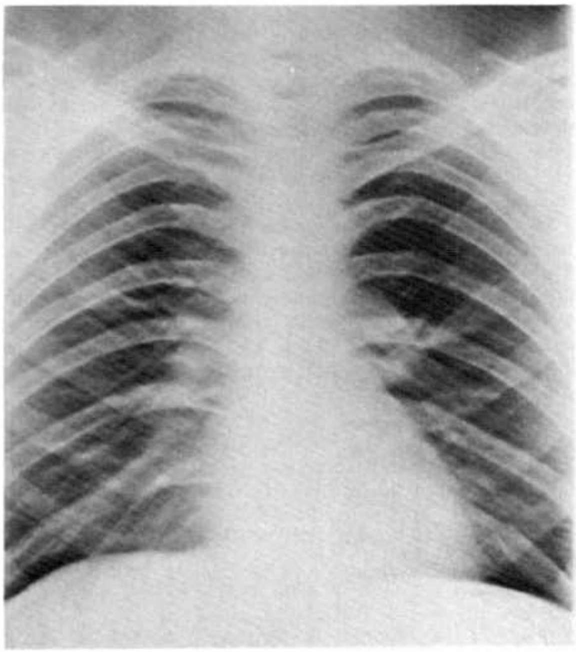

FIG. 1.

Digital chest ionogram displayed at 1600 × 1200 pixels. Exposure factors are 65 kVp, 50 mAs and entrance skin dose 250 μGy (25 mrad).

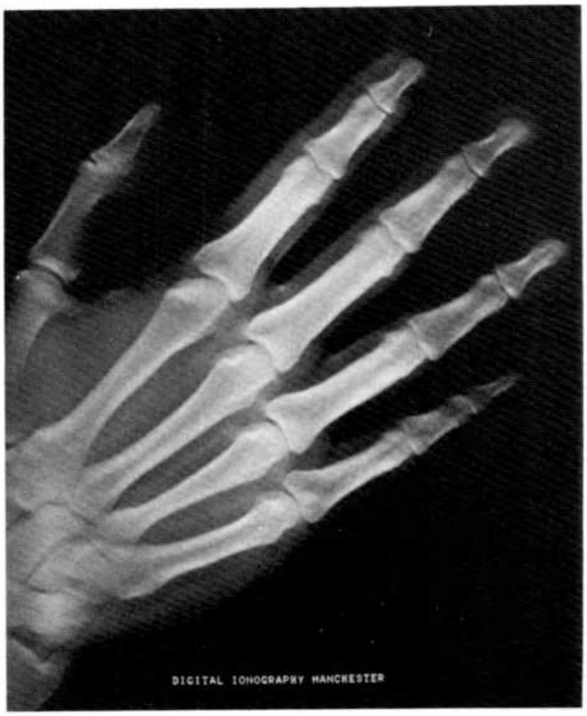

FIG. 2.

Digital ionogram displaying over 3 line pairs per mm resolution.

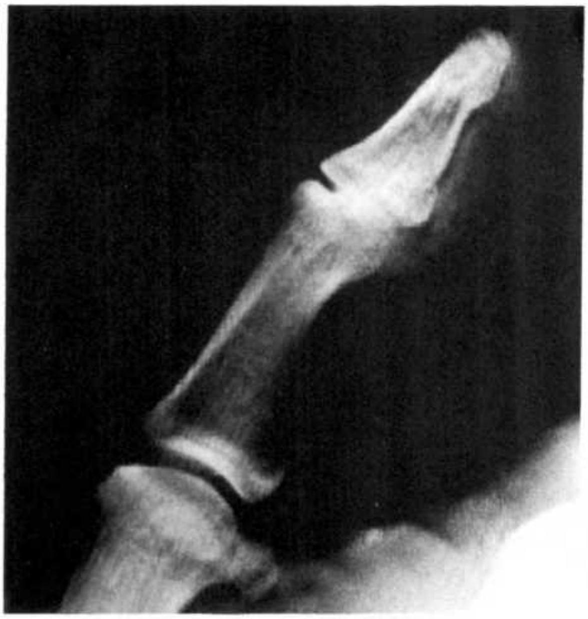

FIG. 3.
Electronic enlargement by a factor of two of an area of image shown in Fig. 2.

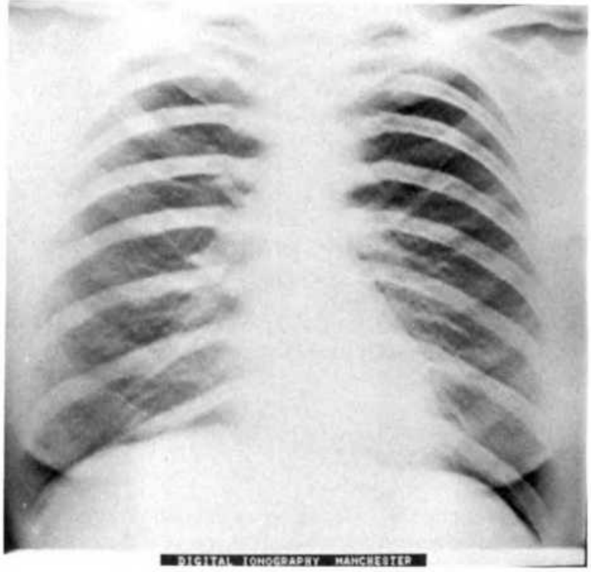

FIG. 4.
Digital chest ionogram employing 72 kVp and 18 mAs exposure factors and corresponding to an entrance skin dose of 170 μGy (17 mrad).

RESULTS AND DISCUSSION

A digital ionography chest image is shown in Fig. 1. This image was produced with exposure factors 65 kVp and 50 mAs on a single-phase X-ray unit at a focus–film distance of 2 m and corresponds to an entrance skin dose of approximately 250 μGy (25 mrad). The overall noise level in this picture is dictated by quantum statistics and the resolution limit of approximately 2 line pairs per mm is mainly governed by the display matrix size, *i.e.* the 40 cm × 30 cm field size sampled at 1600 × 1200 pixels corresponds to four data points per mm.

The apertures of the electrometers used to read the electrostatic images are roughly 0.15 mm in diameter and correspond to a resolution limit in excess of 4 line pairs per mm at the electrometer-to-foil spacing employed. However, these samples are displayed onto a pixel size of 0.25 mm. This means that it should be possible either to increase the aperture of the electrometers, and thus increase the signal-to-noise ratio, for the same overall resolution, or the resolution can be increased for the same signal-to-noise ratio. The latter is demonstrated in Fig. 2, where a smaller input field size (roughly 17.5 cm × 17.5 cm) has been sampled on the 1200 × 1200 pixel matrix. The resolution limit in this image is now approximately 3.4 line pairs per mm, which has been measured by means of a lead-bar pattern image. This level of resolution and sensitivity is now comparable with that of screen–film systems. However, given the technical developments possible with ionography systems the imaging capability shown by this prototype unit can be greatly increased.

One of the potential advantages of digital imaging is highlighted in Fig. 3, where a portion of the image presented in Fig. 2 has been electronically magnified by a factor of two and the visualisation of fine detail is clearly demonstrated. It must be noted that, because the ionography process is linear, all the grey-scale detail present in an image cannot be viewed simultaneously. In all the images presented, window width and height functions were employed in order to present what was deemed to be a suitable image, which was then photographed from the visual display unit.

Clinical evaluation and further development of the system is under way. Part of this evaluation will involve a comparison with a rare-earth screen–film combination. That the system as presently designed can compete with rare-earth screen–film combinations in terms of speed is indicated in Fig. 4. This image employed exposure factors 72 kVp and 18 mAs on a three-phase unit and corresponds to an entrance skin dose of 170 μGy (17 mrad), similar to that employed on the screen–film combination.

Obviously, the results presented are preliminary but, hopefully, do demonstrate the potential of this technique. There is scope for major development of the existing system to improve greatly both the sensitivity and resolution, as well as to enhance greatly its operation with patients. The technology is also simple and cheap—the cost per image produced can be a fraction of the equivalent film costs.

ACKNOWLEDGMENTS

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Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Magnetic resonance flow imaging: a possible method for distinguishing communicating syringomyelia from cystic intraspinal lesions

THE EDITOR—SIR,

The important radiological differential diagnosis of syringomyelia is an intramedullary tumour. Magnetic resonance (MR) is now the modality of choice to image the spinal cord and canal (Han et al, 1983; Yeates et al, 1983; Norman et al, 1983). However, differentiation between the cerebrospinal fluid (CSF) contained within a syrinx and a cystic tumour is a potential problem, as there may be little difference in the relaxation parameters (T_1 and T_2) or in the morphology. One possible means of differentiating these conditions is to study CSF flow using a MR phase imaging technique (Ridgway & Smith, 1986; Ridgway et al, 1987), which has recently been developed to allow quantitative measurement of flow velocities, including low values found in CSF flow.

We recently studied a 38-year-old lady who presented with a history of mild spinal-cord disturbance, suggestive of a demyelinating disease. The MR scan showed a probable syrinx extending from the level of the first cervical vertebra to at least the second thoracic vertebra, with some associated tonsillar herniation (Fig. 1). Although in this case the demonstration of a coexisting Chiari malformation established the diagnosis, phase images were obtained in order to detect CSF flow within the syrinx. These were obtained in the transverse plane at the level of the second cervical vertebra; the pulse sequence was gated from the R-wave of the subject's electrocardiogram and images obtained at 50, 225, 300 and 325 ms following the R-wave. Both the time intervals and choice of level corresponded to those used in a previous study carried out on normal volunteers (Ridgway et al, 1987). The cross-sectional area of the syrinx was measured from the images and maximum caudad and cephalad flow rates and velocities were calculated.

Pulsatile CSF flow was demonstrated within the syrinx during the cardiac cycle (Fig. 2). A maximum caudad flow rate of 1.27 ml s^{-1} was achieved at 300 ms following the R-wave. This corresponds to a maximum velocity of 1.63 cm s^{-1}, which was calculated from the area of the syrinx (0.87 cm^2). Cephalad flow was maximum at 50 ms with a flow rate of 0.64 ml s^{-1} and a velocity of 0.86 cm s^{-1}. Due to cord expansion, the subarachnoid space at the level imaged was too small for accurate measurement of CSF flow outside the syrinx to be obtained.

Magnetic resonance phase imaging offers a means of studying the velocity and direction of flow in both normal and pathological CSF circulation. It may prove to be useful non-invasive technique to distinguish communicating and non-communicating forms of syringomyelia, including those associated with spinal-cord tumours, posterior-fossa tumours or cysts, and spinal-cord trauma.

We would like to thank Dr G. Venables for valuable clinical assistance.

Yours, etc.

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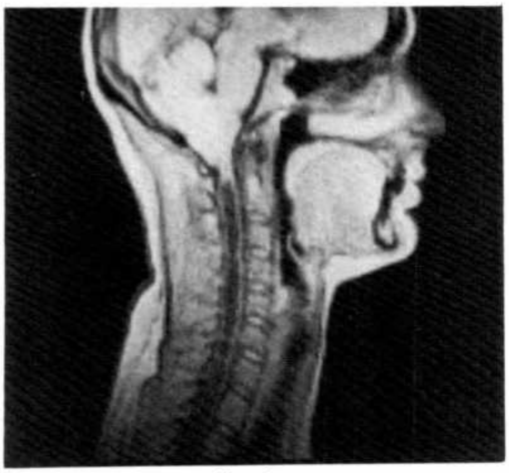

FIG. 1.

Sagittal proton density image showing fusiform enlargement of the spinal cord. The syrinx cavity is identified as a low-intensity area, vertically orientated, running throughout the length of the cord.

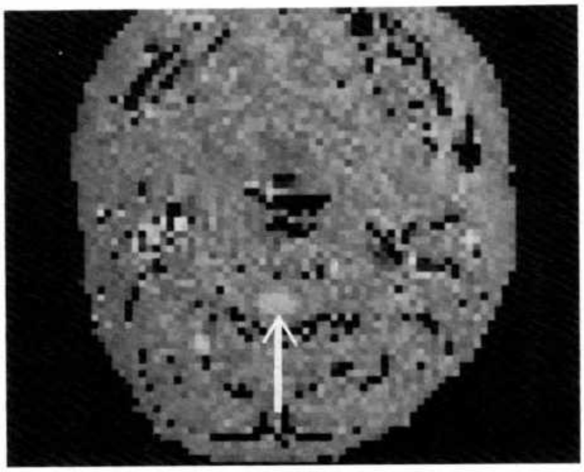

FIG. 2.

Transverse phase image at the level of the second cervical vertebra. The flow within the syrinx is seen as an oval area of increased intensity (arrow). Blood flow within the right deep cervical vein is noted.

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Avoidance of ring artefacts in lumbar spine computed tomography in obese patients

THE EDITOR—SIR,

Central ring artefacts (Kowalski & Wagner, 1977) are sometimes unavoidable on computed tomography (CT) in very obese patients, even when meticulous care has been taken with calibration (Seeram, 1982). This is because of low photon transmission and consequent low signal-to-noise ratio (Haaga et al, 1981). The spinal canal is often at the precise centre of the axis of tomographic rotation and, thus, especially liable to be obscured by such artefacts (Fig. 1). This can be avoided by purposely positioning the patient slightly off centre within the gantry aperture so that the spinal canal is removed from the axis of rotation (Fig. 2).

Quantum mottle on the initial lateral scanogram is indicative of low photon transmission and provides a clue that deliberate off-centring may be beneficial.

Yours, etc.,
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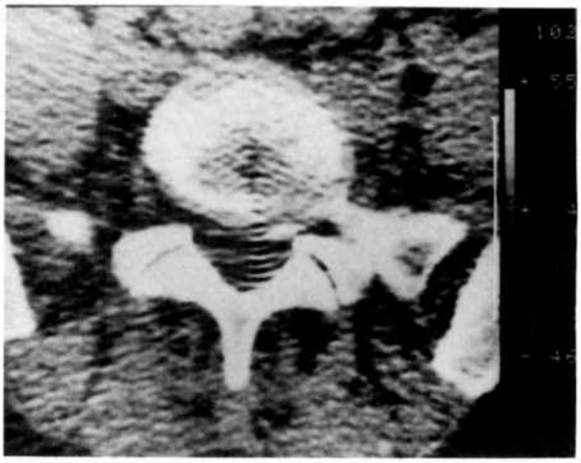

FIG. 1.

Computed tomogram of the L5/S1 disc of an extremely obese patient (W = 1024, L = +45). A central field of reconstruction has been used with a magnification factor of 4.2. The central ring artefacts obscure detail of the disc.

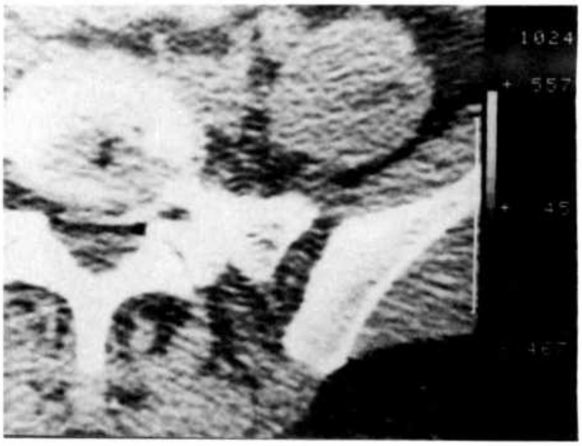

FIG. 2.

The patient has been moved 3.5 cm to the right. The ring artefact is now over the left sacral alum. The degenerate L5/S1 disc is seen more clearly.

Obituaries

Professor J. S. Mitchell, C.B.E., F.R.S.

Professor J. S. Mitchell died on February 22, 1987, at the age of 77. Over the entrance to his research laboratories, where he was still active until a few months before his death, there was a notice that read "The aim of this department is to improve the treatment of cancer". This notice dated from 1946 when it had been put up in the entrance lobby of the University Department of Radiotherapeutics at the time when Joseph Mitchell was appointed to the newly created Chair. The sentence states succinctly the cause to which he devoted the major part of his working life.

Joseph Stanley Mitchell was born in 1909 to schoolteacher parents in Birmingham, and started on the educational ladder at Marlborough Road Council School. At the age of eight he gained an entrance scholarship to Camphill Grammar School and four years later, by a further entrance scholarship, he transferred to the King Edward VI High School. There he was on the classical side until his last two years and, in fact, continued Latin until leaving.

As a youngster he was greatly affected by the sufferings of a near neighbour who died of cancer, and the apparent incurability of the disease made a profound impression on him. It was not surprising, therefore, that he decided to study medicine and entered the University of Birmingham Medical School. After completing the preclinical course, he won an open scholarship to St John's College, Cambridge, where he took the Natural Sciences Tripos and obtained a first in physics. He then returned to Birmingham for his clinical studies and qualified by passing the Cambridge Final M.B. Examination in 1933. In the next year he was awarded a Beit Memorial Fellowship and worked for a Ph.D. at the Colloid Science Laboratory in Cambridge. The subject of his thesis was "The photochemistry of proteins". This led to one of his first publications on the effects of radiation on tissue, a paper in the *Proceedings of the Royal Society* entitled "The origin of the erythema curve and the pharmacological action of ultraviolet radiation". An appendix to this paper was written jointly with C. B. Allsopp, who later became an editor of the *British Journal of Radiology* and a President of the Institute.

After this research work, Mitchell worked for a brief period as Resident Radiological Officer at the Christie Hospital, Manchester, and then returned to Cambridge as Assistant in Research in Radiotherapy at the Department of Medicine with clinical facilities at Addenbrooke's Hospital. At the outbreak of war he was in charge of X-ray and radium therapy, and his first contribution to the *British Journal of Radiology* was in 1942 on the measurement of the effects of X and γ irradiation on normal and malignant cells by ultraviolet photomicrography. A paper in the following year discussed the metabolic effects of therapeutic doses of X and γ radiations.

In 1944 he was recruited for the British and Canadian Atomic Energy Project and went to Montreal, where he was in charge of medical investigations. He was particularly concerned with the biological effects of neutrons, and his combined knowledge of physics and medicine was especially valuable. He also looked forward to the possible medical uses of radionuclides in peacetime. When he reviewed these possibilities in a paper in the Journal in 1946, he advocated cobalt 60 as being "eminently suitable for use in radiotherapy". It was therefore most appropriate that, nearly 40 years later, he compiled with Dr Monty Cohen a WHO/ILEA publication *Cobalt 60: A Compendium of International Practice.*

When Mitchell returned to Cambridge to become Professor of Radiotherapeutics at the University and Honorary Director of the Radiotherapeutic Centre, the equipment consisted of two 220 kV X-ray machines and a superficial unit, all housed in a prefabricated hut. In 1946 he had, in collaboration with Dr L. H. Gray, prepared an MRC report on "The therapeutic applications of high energy beta and gamma radiations with special reference to betatrons for voltages up to 50 MeV and the present state of development of linear accelerators". It was natural, therefore, that when two 30 MeV synchrotrons were to be provided for medical purposes, one of them was installed at Cambridge. It was a very "non-clinical" machine, with a fixed beam and a noise level when in operation that necessitated the patients having ear-plugs! Nevertheless, a few patients were treated successfully and some valuable experience was gained in the therapeutic use of high-energy X rays.

From 1947 onwards, much of the research activities of Professor Mitchell and his colleagues was devoted to the study of radiosensitisers, particularly a synthetic vitamin K substitute, Synkavit, which was shown to have a sensitising action in tissue culture and animal tumours. When subjected to clinical trials in patients, however, the effect was disappointingly small. This work on electron-affinic sensitisers provided a stimulus to the very considerable effort devoted to hypoxic-cell radiosensitisers over the past decade. Because of the increased concentration of Synkavit in tumour tissue, Mitchell pursued the possibility of labelling it with a suitable radionuclide so that it could be used for either diagnostic or therapeutic purposes. Both tritium and iodine 131 were tried, with limited success. Since his retirement from clinical work in 1976, he had been actively engaged with colleagues in developing a compound labelled with the α emitter, astatine 211. Preliminary studies in animal tumours had produced encouraging results.

Professor Mitchell was one of the first to recognise the importance of testing new forms of therapy by prospective randomised clinical trials. He therefore initiated trials of Synkavit in patients with lung cancer. He also played a major part in setting up two trials of treatment of early breast cancer. The first was confined to the Cambridge area and compared radical mastectomy plus radiotherapy with simple mastectomy plus radiotherapy in Stage II disease. The second was a large multicentre trial in collaboration with the Department of Surgery at King's College Hospital, and compared simple mastectomy plus radiotherapy with simple mastectomy alone. The results of these two trials have had an important influence on current practice in the treatment of breast cancer.

In 1957 Mitchell was appointed Regius Professor of Physic at Cambridge, but remained head of the Department of Radiotherapeutics and Director of the Radiotherapeutic Centre. He worked hard to have a Clinical School of Medicine in Cambridge and was finally rewarded by seeing this established, although he retired from the Regius Chair in 1975, the year before the first intake of clinical students.

Professor Mitchell had an international reputation and was UK Advisor to the four conferences held at Geneva from 1955 to 1971 on the Peaceful Uses of Atomic Energy. He was held in particularly high regard in Germany where he had active links with universities and was an Honorary Member of the German Röntgen Society. He was a Founder President of the British Section of the Anglo-German Medical Society. In 1951 he was made a Commander of the British Empire and in 1952 a Fellow of the Royal Society, serving on its council from 1955 to 1957. He was Dunham Lecturer at Harvard, Withering Lecturer at Birmingham, a Fellow of the Royal College of Radiologists and, in 1965, gave its Robert Knox Memorial Lecture. He was Silvanus Thompson Memorial Lecturer of the Institute in 1968, and gave the Linacre Lecture in 1970 at St John's College, Cambridge, where he had been a Fellow since 1936. He was a Fellow of the Royal College of Physicians and a Foreign Fellow of the Indian National Academy of Sciences. He was awarded an Honorary D.Sc. of the University of Birmingham in 1958 and the Pirogoff Medal of the USSR Academy of Medical Sciences in 1967.

In spite of his research work and the burden of academic administration, Professor Mitchell always found time for clinical work in which he was completely unsparing of himself. He had an immense concern for the total well being of his patients. This gave him a great interest in the psychological features and needs of cancer patients and he actively supported work in this field by being a member of the Research Committee of the Faith Courtauld Unit at King's College Hospital. His patients loved him and showed it in a practical way by their generous support of his research fund. Paradoxically, but as a result of this highly caring attitude, he admitted that retirement from clinical practice was in some ways a relief for him. It removed a perpetual burden of worry about all his individual patients.

He cared for his staff, not only as colleagues but as people, and was always very understanding of personal problems. He valued the contribution made by people in non-medical disciplines and, perhaps because of his early training in physics, was particularly supportive of the development of medical physics in hospitals. He was made an Honorary Member of the Hospital Physicists' Association in 1949.

Although it might have seemed that his work was his whole life, Professor Mitchell enjoyed modern languages and a good walk. Those who knew him well found that there was a good sense of humour concealed behind his quiet, retiring manner. In recent years he had been interested in local politics and was, for a period, President of the Southeast Cambridgeshire Liberal Association.

Dr Lillian Mary Mitchell, whom he married in 1934, was a great influence on his life and work and gave him constant support. She died in 1983. They are survived by their son, Christopher, and daughter, Janet.

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Honorary Professorship for T. J. Deeley

Dr T. J. Deeley, O.B.E., F.R.C.R., Fi.Biol., Director and Consultant in Administrative Charge, South Wales Radiotherapy and Oncology Service, Velindre Hospital, Cardiff, Lecturer in Radiotherapy, University of Wales College of Medicine, has been made an Honorary Professor in Microbiology, University College, Cardiff.

Members' use of the Toshiba Room

Members may borrow the Toshiba Room free of charge, subject to availability. This conference meeting room seats 16 people with comfort.

Full details from Mrs Anne Clayton, Assistant Secretary: Administration at the BIR.

The BIR Nycomed Scandinavian Scholarships 1988

Applications should be submitted by July 31, 1987, and interviews will take place in September.

For further information please write to: The General Secretary, The British Institute of Radiology, 36 Portland Place, London W1N 4AT.

Dr Robert Ward McNabb

Robert McNabb was born in Lincolnshire, July 31, 1907. He trained at Guy's Hospital where he obtained his M.R.C.S. and L.R.C.P. in 1931. He returned to Lincolnshire as a general practitioner from 1932 until 1949, where he was greatly loved by all who knew him. In 1952 he moved to Guy's Hospital where he obtained his D.M.R.D. He practised radiology at Edgware General, West Herts and St Paul's Hospitals, becoming a consultant radiologist to the Peace Memorial and Shrodells Hospitals Watford in 1959.

Robert always displayed a great interest in the welfare of Watford General Hospital, particularly the Radiology Department. He was a great friend and colleague and although he retired in July 1972 he was still fondly remembered by his staff. He had an excellent relationship with his colleagues, which brought him to prominence within both the medical profession in Watford and the community.

As the Chairman of the Medical Staff Committee he helped with the planning and development of the new Princess Michael of Kent Wing. His drive and enthusiasm for the project was well known at both regional and local levels, and he was an honoured guest at the opening of this wing in February 1986.

His outside interests included travelling, photography and history and he was writing a history of Watford Hospital, sadly unfinished at his premature death. He is survived by his wife Gwen, son Robert and his four grandchildren, Karen, Kevin, Ian and Julia. He was well liked and respected by all who knew him and he will be greatly missed.

T. F. El Sayed

BIR calendar events

Unless otherwise indicated, enquiries about the following events should be addressed to the Assistant Secretary: Programme, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

The meetings are at 36 Portland Place unless otherwise stated. Attendance is open to non-members.

Annual General Meeting
May 14, 1987 at 4.30 p.m.

Imaging in Radiotherapy
May 15, 1987
Chairmen: Dr D. Thwaites and another to be announced.
Topics are expected to include integrated treatment planning, special imaging techniques, radiotherapy portal imaging, three-dimensional imaging and simulator CT.
Joint IPSM/BIR all day meeting organised by IPSM.

Dysphagia and Disorders of Swallowing
May 20, 1987
Royal Society of Medicine, London
Joint RSM/RCR/BIR all day meeting to be organised by the RSM.

Conversazione
May 20, 1987
Royal Naval College, Greenwich

British Institute of Radiology 46th Annual Congress
incorporating the joint BIR/RCR/RSM (Section of Radiology) spring meeting and in collaboration with the Scottish Radiological Society

Radiology '88
Glasgow May 23–25, 1988

Glasgow will be the first in a series of back-to-back meetings with the Annual Conference of the College of Radiographers. The technical exhibition will span both meetings and be the manufacturers' showcase in 1988.

The place: the brand new Scottish Exhibition and Conference Centre.

Radiology '88 will cover all aspects of radiology: X-ray diagnosis, radiation oncology, nuclear medicine, ultrasound, NMR, radiological physics, radiobiology, radiation protection and related disciplines.

Proffered papers and posters are invited: closing date November 30 1987.

Library news

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Thursdays)

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–5 p.m., and Thursdays 11 a.m.–7 p.m., and Mrs Angela Lansdown, daily 9 a.m.–5 p.m. (Tel. 01-580 4085).

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post. A list of current journals is available on request and is also published in the March and September issues of the Bulletin.

Most books (excepting the historical collection) are available on loan.

Recent additions to the Library

Hill, C. R. (Ed.): Physical principles of medical ultrasonics. 1986

Hricak, H. (Ed.): Genito-urinary ultrasound. Clinics in diagnostic ultrasound, Vol. 18. 1986

Lewis, S. M. & Bayly, R. J. (Eds): Radionuclides in haematology. 1986

Lippert, H. & Pabst, R.: Arterial variations in man. Classification and frequency. 1985

Maruyama, Y., Beach, J. L. & Feola, J. M. (Eds): Californium-252 brachytherapy and fast neutron beam therapy. Proceedings of the workshop in Lexington, Kentucky, April 1985

Palmer, P. E. S.: Manual of darkroom technique. WHO basic radiological system. 1985

Swischuk, L. E.: Emergency radiology of the acutely ill or injured child. 2nd edit. 1986

Wells, P. N. T. (Ed.): The safety of diagnostic ultrasound. BJR Suppl. No. 20. 1987

WHO: Guidelines for the study of genetic effects in human populations. Environmental health criteria. 46. 1985

Meetings and courses

As a service to our readers, the title, date and place of meetings and contact address will be inserted free of charge: any additional information will be charged at £1.75 per printed line, per insertion. Please contact the Managing Editor.

Two-Day Course in Endosonography

May 19–20, 1987
Middlesex Hospital, London
Further details: Fiona Graves, KeyMed, KeyMed House, Stock Road, Southend-on-Sea SS2 5QH (Tel. 0702-616 333).

Current Skeletal Radiology

May 22–23, 1987
Granby Hotel, Harrogate, Yorkshire
Further details: Mr B. F. Moran, Postgraduate, Deans Office, Level 7, Worseley Medical and Dental Building, The University, Leeds LS2 9JT.

VI Congress of the European Association of Radiology (ECR '87)

May 31–June 6, 1987
Lisbon, Portugal
Further details: Secretariat ECR '87, SPRMN, Av. Elias Garcia, 123-7° DTo, 1000 Lisboa, Portugal, (Tel: 77-05 30, Telex 62074 SPRMN P).

Chest Tumours

June 22–27, 1987
Como, Italy
Further details: European School of Oncology, Via Venezian 1, 20133 Milan, Italy (Tel. 02 235 923-266 4662).

College of Radiographers' Annual Conference

July 1–3, 1987
Scarborough
Further details: Miss C. Aldridge, College of Radiographers, 14 Upper Wimpole Street, London W1M 8BN (Tel. 01-935 5726, ext. 206).

Disorders of Bone—Clinical Problems and Imaging Solutions

July 1–8, 1987
Alaska
Further details: Ryals and Associates, P.O. Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Medical Oncology

July 5–11, 1987
Como, Italy
Further details: European School of Oncology, Via Venezian 1, 20133 Milan, Italy (Tel. 02 235 923-266 4662).

Ultrasound (Doppler) and Interventional Radiology—the "Cutting Edge"

July 25–August 1, 1987
St Thomas, Virgin Islands
Further details: Ryals and Associates, P.O. Box 920113, Norcross, GA 30092-0113, USA (Tel. 404-641 9773).

Paediatric Radiology Course

September 2–4, 1987
A course for consultants and senior registrars oriented to solving the basic paediatric problems they are likely to meet in a DGH. Also suitable for FRCR candidates.

Further details: Dr G. M. Steiner, Sheffield Children's Hospital, Western Bank, Sheffield S10 2TH (Tel. 0742-761111).

Symposium Mammographicum

September 3–4, 1987
Nottingham
Further details: The Conference Officer, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG (Tel. 01-636 4432/3).

St Bart's Megavoltage Radiotherapy 50th Anniversary Conference

September 3–5, 1987
St Bartholomew's Hospital, London
Further details: The Secretariat, Concorde Services, 10 Wendell Road, London W12 9RT.

HPA Annual General Meeting and IPSM Scientific Meeting

September 15–19, 1987
Liverpool
Further details: IPSM, 47 Belgrave Square, London SW1X 8QX (Tel. 01-235 6111).

14th Annual Refresher Course of the International Skeletal Society

September 16–19, 1987
Cannes, France
Further details: Ms Janice Ford, Convention Manager, International Skeletal Society, 39 Dunlin Way, Eriao, New Jersey 08081, USA (Tel. 213-662 6904).

RCR Annual Meeting and Annual General Meeting

September 24–26, 1987
John Radcliffe Hospital, Oxford
Incorporating the Joint Autumn Provincial Meeting of the RCR, the BIR and the Radiology Section of the RSM
Further details: The Conference Officer, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG (Tel. 01-636 4432/3).

12th Annual International Body Imaging Conference

October 10–18, 1987
Maui, Hawaii
Further details: Medical Seminars International, 21915 Roscoe Boulevard, Suite 222, Canoga Park, CA 91304, USA (Tel. 818-340 0580 ext. 280).

6th Symposium on Neutron Dosimetry

October 12–16, 1987
Neuherberg, Federal Republic of Germany
Further details: GSF München, Institut für Strahlenschutz, Dr H. Schraube, Ingolstädter Landstr. 1, D-8042 Neuherberg, Federal Republic of Germany (Tel. 089-31 87 (0) 3349).

Post-RSNA Imaging

December 5–12, 1987
Caribbean cruise
Further details: Medical Seminars International, 21915 Roscoe Boulevard, Suite 222, Canoga Park, CA 91304, USA (Tel. 818–340 0580 ext. 280).

11th International Congress of Head and Neck Radiology

June 6–11, 1988
Uppsala, Sweden
Further details: H. Wilbrand, M.D., Department of Diagnostic Radiology, University Hospital, S-751 85 Uppsala, Sweden.

Annual Meeting and Postgraduate Course

June 12–17, 1988
West Berlin
Arranged by the Cardiovascular and Interventional Radiological Society of Europe and the American Society of Cardiovascular and Interventional Radiology
Further details: Reingard Sörensen, M.D., Klinikum Steglitz, Röntgendiagnostik, Hindenburgdamm 30, 1000 Berlin 45, Federal Republic of Germany.

The British Institute of Radiology Nycomed Scandinavian Scholarships 1988

The British Institute of Radiology invites applications for the 1988 Nycomed Scandinavian Scholarships.

These Scholarships, which are generously funded by Nycomed (UK) Ltd, enable United Kingdom diagnostic radiologists, preferably members of the British Institute of Radiology, to visit Scandinavian academic departments for up to two months' concentrated study, free of financial constraints: a maximum of £2500 per month will be provided.

The purpose of the Nycomed Scandinavian Scholarships is to enable diagnostic radiologists of senior registrar or junior consultant status, interested in diagnostic or interventional procedures concerned with intravascular contrast media, to visit one or more academic departments of radiology in Scandinavia (Norway, Sweden, Denmark) for in-depth radiological experience of up to two months. Each recipient will be responsible for his/her itinerary, travel, accommodation and insurance arrangements, subject to the approval of the BIR.

A condition of each scholarship is that a report of work undertaken, in a form suitable for publication in the Bulletin of the British Institute of Radiology, shall be submitted.

Applications for 1988 should be submitted by **31 July 1987** and interviews will take place in September.

Nyegaard (UK) Limited wishes to announce there has been a change of Company name to : NYCOMED (UK) LIMITED.

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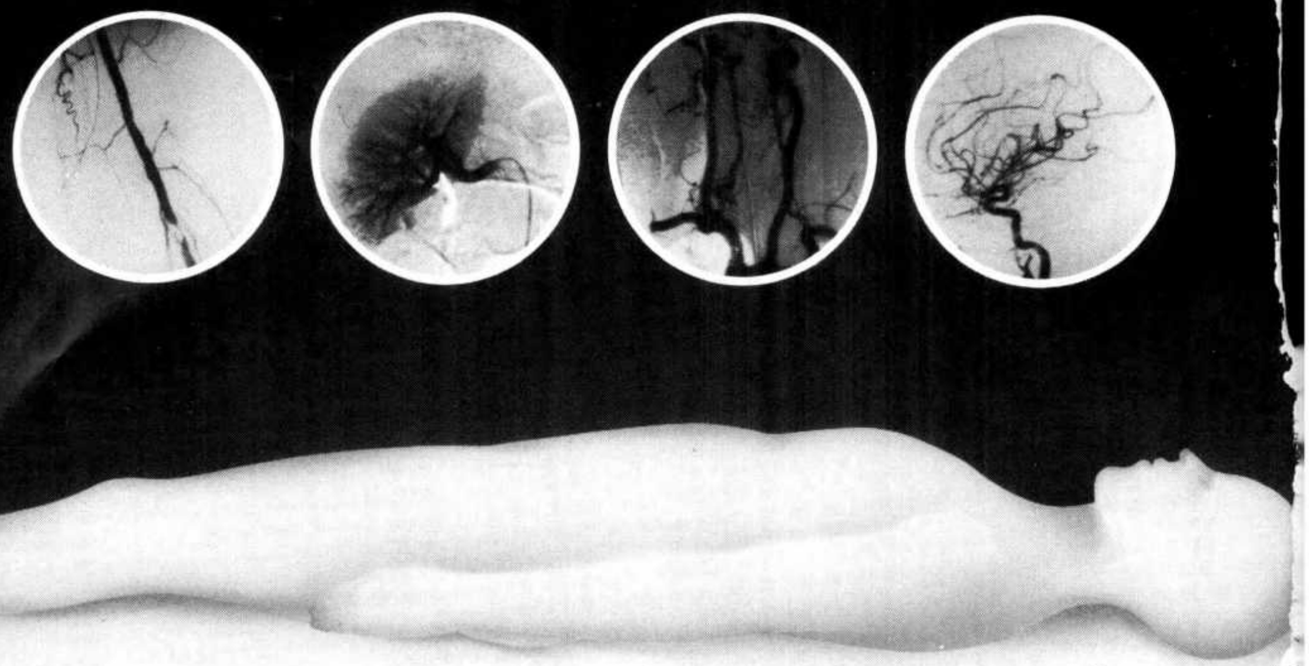

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